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ÜLLE VÕHMA

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Association between personality traits, clinical characteristics and pharmacological treatment response in panic disorder

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Department of Psychiatry, Institute of Clinical Medicine, University of Tartu, Tartu, Estonia

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Supervisors: Eduard Maron, MD, PhD, Professor,
Department of Psychiatry, Institute of Clinical Medicine, Faculty of Medicine, University of Tartu, Tartu, Estonia

Anu Aluoja, PhD, Associate Professor,
Department of Psychiatry, Institute of Clinical Medicine, Faculty of Medicine, University of Tartu, Tartu, Estonia

Innar Tõru, MD, PhD, Associate Professor,
Department of Psychiatry, Institute of Clinical Medicine, Faculty of Medicine, University of Tartu, Tartu, Estonia

Reviewers: Jaanus Harro MD, PhD, Professor and Head,
Department of Neuropsychopharmacology, Institute of Psychology, Faculty of Social Sciences, University of Tartu, Tartu, Estonia

Kirsti Akkermann PhD, Associate Professor,
Department of Clinical Psychology, Institute of Psychology, Faculty of Social Scienes, University of Tartu, Tartu, Estonia

Opponent: Virginija Adomaitiene, MD, PhD, Professor, Head of Psychiatry Department, Lithuanian University of Health Sciences, Medical Academy, Kaunas, Lithuania

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LIST OF ORIGINAL PUBLICATIONS

This thesis is based on the following original publications, which are referred to in the text by Roman numerals I–III.

I Aluoja A, Voogne H, Maron E, Gustavsson P, **Võhma Ü**, Shlik J. Personality traits measured by the Swedish universities Scales of Personality: Factor structure and position within the five-factor model in an Estonian sample. *Nordic J of Psychiatry* 2009; 63 (3): 231–236.

II **Võhma Ü**, Aluoja A, Vasar V, Shlik J, Maron E. Evaluation of personality traits in panic disorder using Swedish universities Scales of Personality. *J Anx Disord* 2010; 24: 141–146.

III **Võhma Ü**, Raag M, Tõru I, Aluoja A, Maron E. Association between personality traits and escitalopram treatment efficacy in panic disorder. *Nordic J of Psychiatry* 2017; 4: 1–8.

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Publication III: Participation in setting the aims and designing the study; organising the study and collecting the data; participation in analysis of the data; interpretation of results; writing the manuscript as the main author.

ABBREVIATIONS

APA	American Psychiatric Association
BPD	Bordeline Personality Disorder
CBT	Cognitive Behavioural Therapy
CCK	Cholecystokinin
CGI	Clinical Global Impression scale
CGI-I	Clinical Global Impression – Improvement scale
CGI-S	Clinical Global Impression – Severity scale
CI	Confidence Interval
CSF	Cerebrospinal Fluid
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders(4th Edition)
ED	Emergency Department
EST-Q	Emotional State Questionnaire
HAM-A	Hamilton Anxiety Scalet
5-HTTLPR	the serotonin transporter gene-linked polymorphism
ICD-10	the International Statistical Classification of Diseases, 10th Revision
KSP	the Karolinska Scales of Personality
MINI	Mini-International Neuropsychiatric Interview
N	Neuroticism
NEO-PI-R	Revised Neuroticism-Extraversion-Openness Personality Inventory
OR	Odds ratio
PD	Panic disorder
PDSS	Panic Disorder Severity Scale
SNRI	Selective Serotonin-Norepinephrine Reuptake Inhibitor
SSP	the Swedish universities Scales of Personality
SSRI	Selective Serotonin Reuptake Inhibitors
SSTI	selektiivne serotoniini tagasihaarde inhibiitor
TCI	Temperament and Character Inventory
TSES	Toronto Side-effect Scale

1. INTRODUCTION

Panic disorder (PD) was officially introduced into the psychiatric nomenclature as a distinct illness in 1980 with the publication of the Diagnostic and Statistical Manual of Mental Disorders, third edition (APA, 1980). The central clinical features of PD are spontaneous panic attacks, involving numerous psychological and physical symptoms. PD is generally considered a chronic or intermittent psychiatric condition which is often disabling (Keller et al., 1994, Batelaan et al., 2010). The illness leads to an increased use of health care services (Rief et al., 2005) as well as a significant loss in the quality of life and psychosocial functioning (Keller et al., 1994, Kessler et al., 2006; Roy-Burne et al., 2006, Mendlowicz et al., 2000).

Genetic, biological, environmental and psychosocial factors, including personality traits were found to play an important role in the development of the PD and influence treatment response (Andrisano et al., 2012, Carrera et al., 2006). Furthermore, a study by Powers and Westen (2009) produced results that suggest the importance of personality in understanding the different phenotypes of panic patients (high functioning, emotionally dysregulated, inhibited/ avoidant, somatizing patients) and in making better predictions about responses to treatment (Powers, 2009). This point of interest was an important motivator for this dissertation.

The expression of personality traits mainly related to anxiety and mood disorders is proposedly connected to serotonin mechanisms (Takano et al.2007). High levels of Neuroticism have been associated with increased serotonin binding within the thalamus (Takano et al.,2007) and $5HT_{1A}$ receptor (Hirvonen et al., 2015)

Personality traits can have some influence on the outcome of pharmacotherapy, which in turn can produce changes in personality. Studies have revealed contradictory results. Some initial reports on PD have indicated that a large improvement in panic symptoms after anxiolytic medication with alprazolam or diazepam is accompanied by significant changes in neuroticism-related personality traits (Reich et al., 1991, Noyes et al., 1986). On the contrary, studies by Carrera et al. (2006) postulated that none of the personality traits of panic disorder patients, assessed by the Neuroticism-Extraversion-Openness Five-factor Personality Inventory (NEO-FFI) were related either to clinical severity or to a short-term response to SSRI treatment (Carrera et al., 2006).

The relation between personality traits and the treatment outcomes of PD remains an important topic for physicians because, although progress has been made in the development of effective pharmacological and psychotherapeutic interventions, still not all patients respond to treatment (Katon et al., 2006). The high rate of treatment failure and relapses in treating PD patients possibly suggest personality diathesis (Powers and Westen, 2009). A more effective comprehension of the relationship between personality factors and PD can help to give a greater understanding of etiology, identify patients at risk of suffering

from more resistant symptoms, and help to both plan treatment and prevent these conditions.

The impact of personality traits on the risk of panic disorder and on its treatment, as well as the stability of a personality disorder diagnosis, has continually been an object of discussion (Johnson et al., 2006; Mennin et al., 2000).

2. REVIEW OF THE LITERATURE

2.1. Clinical characteristics and course of panic disorder

Panic disorder (PD) is a serious anxiety disorder characterised by recurrent panic attacks and associated fearful anticipation of panic and its consequences, and frequently developing agoraphobia (DSM-IV, ICD-10). Panic attacks are defined as rapidly escalating occurrences of at least four out of 13 distressing symptoms including palpitations, sweating, trembling or shaking, shortness of breath or smothering, feeling of choking, chest pain or discomfort, nausea or abdominal distress, feeling dizzy, unsteady, lightheaded, or faint, derealisation, depersonalisation, fear of losing control or going crazy, fear of dying, paresthesias and chills or hot flushes. The identification of PD requires careful differential diagnosis from panic-like symptoms and autonomic arousal resulting from the direct physiological effects of substance use or a general medical condition and from symptoms of anxiety better explained by another mental health disorder. On the other hand, patients with PD have an increased risk of other psychiatric as well as medical morbidity. There is a high degree of PD comorbidity with other mental health disorders: 30–63% for major depression, 29.5–58.2% for agoraphobia, 20–75% for social phobia, 20% for generalised anxiety disorders, 14% for obsessive-compulsive disorder, 13% for bipolar disorder and 6% for post-traumatic stress disorder (Goisman et al., 1994; Chen and Dilsaver, 1995; Pelissolo and Lepine 1998; Eaton et al., 1994; Wittchen et al., 1998; Weissman et al., 1997; Kessler et al., 1998; Kessler et al., 2006; Lamers et al., 2011; Preti et al., 2018). Substance abuse is also a common comorbid disorder in up to 36% of cases according to Epidemiological Catchment Area data (Regier et al., 1998). In addition, PD often occurs together with cardiac, gastrointestinal, respiratory and neurological disorders (Zaubler and Katon, 1998).

According to epidemiological surveys, sporadic panic attacks occur in the population at 7–15% the lifetime prevalence rate (Pelissolo and Lepine, 1998; Eaton et al., 1994), and are often associated with substantial morbidity even in the absence of a full clinical manifestation of PD (Klerman et al., 1991). The lifetime prevalence of PD rates are between 1.5% and 3.5%, while twelve-month prevalence rates in females were found to be higher than in males (Eaton et al., 1994). In Estonia, the prevalence of panic symptoms among primary care patients is different among men and women, accordingly 5.5% for men and 8% for women (King et al., 2008) – a tendency that has been demonstrated in several studies. The age of onset of PD is usually in the mid-twenties, with hazard rates for females ranging from 25 to 34 years and for males between 30 and 44 years (Wittchen and Essau, 1993). As with gender, data about PD is also different with age. Panic attacks were observed in 3% of youths aged from 9 to 17 years (Goodwin and Gotlib 2004) and PD was diagnosed in 10–13% of clinically referred children and adolescents (Doerfler et al., 2007, Masi et

al.,2000). Lower rates of panic disorder are typically seen in persons aged 65 and older (Robins, 1991, Kessler et al., 2006, Yates, 2009).

PD has been recognised as a chronic condition with a fluctuating course (Liebowitz 1997; Pollack and Otto, 1997). Some studies have addressed longitudinal aspects; for example, in a three-year follow-up only 10% of patients with PD were symptom-free (Noyes et al., 1990) and only 12% of PD patients were in full remission after five years (Faravelli et al., 1995). At follow-up, study revealed that 25–50% of PD patients relapse within 6 months after discontinuation of drug treatment (Pull and Damsa, 2008). There is evidence that the more important predicting factors of the course of panic disorder in the clinical population are not the severity and frequency of panic attacks, but rather long duration and agoraphobia at baseline (Katschnig and Amering, 1998). Predictors of remission were found to be female gender, the absence of ongoing difficulties, subthreshold panic and a low initial frequency of attacks (Katon, 1987, Kessler 2006).

PD can be a seriously disabling disorder that causes impairment in social, personal and occupational functioning and a significant loss of quality of life (Candilis et al., 1999). The rate of those PD patients who are dependent on welfare or disability benefits exceeds 25% in some studies (Katerndahl and Realini, 1997). Furthermore, medical utilisation rates among individuals with panic disorder appear disproportionately high (Barsky et al., 1999; Katerndahl and Realini, 1997, Zane et al., 2003). Panic disorder patients consulted their general practitioner significantly more often than the control group (Simpson et al. (1994). More frequent physician visits, emergency room visits and mental health visits were reported among patients with PD as compared to general medical outpatients (Barsky et al., 1999). Patients seek immediate medical care during initial panic attacks, commonly in the Emergency Department (ED), because these attacks are often interpreted as evidence of a catastrophic physical disorder, such as a myocardial infarction (Tueth, 1997; Dammen et al., 2001) or respiratory failure and uncomfortable feelings related to fear of death. This is the reason why patients who screen positive for panic disorder use emergency medical services and ED services more frequently (Zane et al., 2003) than the general population. Although only 60% of people with panic disorder seek care, 32% of these patients present to EDs (Zun, 1997, Fleet et al., 1996). Approximately 35% of patients with PD visit their general family practitioner and continue to receive treatment with their primary physician, while only 26% of panic attack patients initially seek care in a mental health setting (Katerndahl and Realini 1995).

2.2. Risk factors of panic disorder

The pathogenesis of PD is complex and involves sociodemographic, psychological, biological and evolutionary factors. Marital status is a significant risk factor for PD: the highest lifetime prevalence rates are found in widowed, separated or divorced subjects (Wittchen and Essau 1993). In particular, about 25% of subjects with PD had a previous divorce, compared to approximately 10% of those with no active phase of disorder (Yates, 2009). There are no consistent findings concerning the educational level and the risk of developing PD, although Eaton et al. (1994) reported a tenfold higher risk for persons with less than 12 years of education. A high frequency of stressful life events also often precedes the onset of PD (Scocco et al., 2007). Several studies have suggested that life events such as early parental loss or childhood abuse may increase the risk of PD (Faravelli 1995; Tweed et al., 1989; Cougle et al., 2010, Goodwin et al., 2005b, Roy-Byrne et al., 1986; Assellmann et al., 2017). Furthermore, children with behavioural inhibitions may appear to have an increased risk for later development of PD (Reznick et al., 1992; Hirshfeld-Becker et al., 2008).

According to the cognitive theory of Clark (1986), individuals who experience recurrent panic attacks have a relatively enduring tendency to interpret certain bodily sensations in a catastrophic fashion. Barlow (1988) described panic as the basic emotion of fear, which is considered to be an acute reaction to perceived imminent danger when no danger is present. The false suffocation alarm theory by Klein (1993) suggested that PD patients have a low stimulation threshold of the asphisiostat, a physiological mechanism of protection from potentially lethal stimuli. One important vulnerability factor for anxiety disorders, and in particular for PD, is anxiety sensitivity or fear of anxiety symptoms. Studies support the idea that anxiety sensitivity acts as cognitive predisposition for the development of PD (Schmidt et al., 1997). Gorman et al. (1989) were the first authors to propose a neuroanatomical model specific to PD. This aetiological model of PD suggested an abnormal sensitivity in the brain mechanism of a fear and alarm response involving a network of neuronal pathways and multiple neurotransmitter systems. According to this hypothesis, panic attacks originate from a dysfunction in the brain fear network that integrates various structures of the brainstem, hippocampus, amygdala, medial hypothalamus, thalamus and cortical regions. This model links acute panic attacks to the brain stem nuclei, anticipatory anxiety to limbic activation and kindling, and phobic avoidance to prefrontal cortical function, integrating biological and psychological aspects of PD (Gorman et al., 2000).

2.3. Pharmacotherapy of panic disorder and treatment outcome

Five classes of medication have been shown in randomised trials to be more effective than placebo in patients with panic disorder: selective serotonin-reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), high-potency benzodiazepines, tricyclic antidepressants and monoamine oxidase inhibitors (Mitte, 2005; Bradwejn, 2005; Otto et al., 2001; Gould et al., 1995; Susman and Klee 2005; Goddard et al., 2001). A meta-analysis compared the efficacy of three pharmacologic classes of medications with placebo in patients with panic disorder as measured by levels of global anxiety (frequency of panic attacks, and agoraphobia) and depression: SSRIs (in 17 trials), tricyclic antidepressants (in 23 trials) and benzodiazepines (in 25 trials) (Mitte, 2005). The three classes of medication were equally effective in treating anxiety, but the effect of benzodiazepines in treating depression was marginally less than that of either tricyclic antidepressants or SSRIs (Mitte, 2005). Large studies have shown a clinically significant response (defined by a 50% decrease in the frequency of panic attacks or global anxiety) in 50 to 80% of patients treated with SSRIs, tricyclic antidepressants or benzodiazepines (Mitte, 2005). An earlier meta-analysis compared the effects of SSRIs or placebo in 12 randomised, controlled trials (Otto et al., 2001). SSRIs were significantly more effective than placebo in reducing global anxiety and the frequency of panic attacks; more than 50% of patients treated with SSRIs became panic-free in seven of nine studies reporting this outcome. In a large, placebo-controlled trial in patients with panic disorder, SNRI venlafaxine, at a dose of 75 to 225 mg per day, reduced the global severity of panic, anticipatory anxiety, and fear and avoidance of social activities on the basis of validated anxiety scales. However, the drug did not increase the likelihood of becoming free of panic (Bradwejn et al., 2005). Because of their safety profile, as compared with the safety profiles of tricyclic agents and monoamine oxidase inhibitors, SSRIs are recommended as the first drug option in the treatment of panic disorder (Otto et al., 2001, Working Group on Panic Disorder 1998). Because clinical experience suggests that many patients with panic disorder are hypervigilant regarding side effects, SSRIs should be started at low doses, with dose titration every five to seven days, as tolerated. Although the benzodiazepines continue to have an important role in the treatment of panic disorder, concern with respect to dependence, medication abuse, side effects, and the rapid re-emergence of symptoms after discontinuation have led to the recommendation that these agents should not be the first choice for treatment, but instead used “as needed” (Susman and Klee 2005).

The goal of treatment should be to eliminate panic attacks, if possible, because a partial response often results in continued avoidance of frightening situations and impairment in social functioning. Unfortunately, not all panic patients achieve remission, so under-treatment of PD remains a major problem (Lydiard,

2011). The literature review shows that 20–40% of PD patients treated pharmacologically are unresponsive to therapies, similar to the 30–40% of patients treated with cognitive-behavioural therapy (van Apeldoorn et al., 2008). Even the integrated therapies are not able to substantially reduce the percentage of insufficient response in PD (van Apeldoorn et al., 2008). In short-term clinical trials, despite the different treatment options, 17–64% of participants with PD did not respond adequately to pharmacotherapy and continued to have PAs and/or exhibited negative behaviour related to PAs (Freire et al., 2016). Furthermore, follow-up studies demonstrate that 25–50% of patients relapse within 6 months after discontinuation of drug treatment, whereas 40–60% of PD patients show subclinical symptoms after 4–6 years of follow-up (Perna et al., 2012; van Apeldoorn, 2008). At 12-year follow-up, patients with panic disorder without agoraphobia were most likely to show a recovery in all assessment points; however, rates of recurrence were similar for panic disorder both with and without agoraphobia (Bruce et al., 2005). Severe agoraphobic avoidance and the severity of depressive symptoms, particularly the recurrent form, are among the predictors of non-remission and poorer outcomes in PD patients (Bruce et al., 2005; Park et al., 2012; Batelaan et al., 2010, Slaap and den Boer, 2001), along with co-morbidity with generalised anxiety disorder, or social phobia and severity of panic symptoms (Chavira et al., 2009), as well as the coexistence of PD and bipolar disorder (Lee, 2008). On the other hand, PD patients without agoraphobia had higher recovery rates, spent considerably less time in illness episodes and were less affected by comorbid conditions compared with patients with any of the other anxiety disorders (Bruce, 2005).

2.4. Personality and panic disorder

Personality is defined as the unique psychological qualities of an individual that influence a variety of characteristic behaviour patterns (both overt and covert) across different situations and over time (Gerrig and Zimbardo, 2002). Personality traits are defined as highly stable behaviour patterns (Kipper et al., 2009), traditionally conceptualised as having two components: temperament, which refers to biologically based, stable individual differences in emotion and its regulation, and character, which refers to individual differences due to socialisation. However, as the distinctions between these constructs are questionable, the terms “personality” and “temperament” are now often used interchangeably (Caspi and Shiner 2006, Clark and Watson 1999). In recent years, some authors have questioned this stability, suggesting that personality characteristics can be influenced by acute psychiatric symptoms and by time frame (Seviewright et al., 2002, Cohrs et al., 2008). Personality characteristics have been described as dynamic constructs that develop over the lifespan and change in response to maturation and life circumstances (Fraley and Roberts 2005, Rothbart and Bates 2006). A number of processes and factors contribute to stability and a change of personality. For example, genes are a considered as a main influence on

phenotypic stability of personality (Krueger and Johnson 2008, Kandler et al., 2010). On the other hand, many of the mechanisms hypothesised to cause personality change (e.g., life events, the timing of various social roles, physical health and cultural values) can differ considerably across cultures (Chopik WJ, Kitayama S. 2018). A recent review showed that personality traits, especially Neuroticism and Extraversion, could change as a result of clinical interventions (Roberts et al., 2017). In contrast to personality traits, which are described in dimensional terms (i.e. less vs. more of a trait), specific personality disorders are instead categorical terms (i.e. presence vs. absence of "disorder") (Brandes et al., 2006) and represent a severe disturbance in the characterological constitution and behavioural tendencies of the individual, usually involving several areas of the personality, and nearly always associated with considerable personal and social disruption. Personality disorder tends to appear in late childhood or adolescence and continues to manifest into adulthood.

The several models aim to explain the relationship between personality traits and major psychiatric disorders, such as depression and PD (Akiskal et al.1983, Klein et al., 2011, Clark et al., 1994, Freire et al., 2007, Krueger and Tackett, 2003, Wachleski et al., 2008). In particular, the following models were proposed by Klein et al. (2011):

(a) The continuous/spectrum model, which considers that personality traits and major psychiatric disorders are epiphenomena of the same process, and the relationship between them is not hierarchical. This model proposes that associations between personality and psychopathology are found because these two constructs both occupy a single domain or spectrum, and psychopathology is simply a display of the extremes of normal personality function. Support for this model is provided by an issue of criterion ovrlap. For instance, two of the primary facet scales of neuroticism are "depression" and "anxiety". Thus, the fact that diagnostic criteria for depression, anxiety and neuroticism assess the same content increases the correlations between these domains.

(b) The precursor model, in which mental disorders and personality have similar etiology, personality predicts onset of disorder.

(c) The common cause model proposes that Neuroticism and common mental disorders, such as depression and anxiety disorders, are related, though not directly, and they share etiology accounts, genetic and environmental determinants.

(d) The "scar" hypothesis, in which the occurrence of mental disorders, such as PD and depression, could provoke permanent personality alterations, such as increased dependency or insecurity (Akiskal et al., 1983, Ormel et al., 2013). According to the scar model, episodes of a mental disorder 'scar' an individual's personality, changing it in significant ways from premorbid functioning. An example of a scar effect would be a decrease in openness to experience following an episode of post-traumatic stress disorder.

(e) The concomitant model proposes mental disorders shape personality and neuroticism, but the effect of psychopathology is temporary. After the episode has remitted, the effect disappeared.

(f) The pathoplasticity model views personality having a causal influence on depression after onset.

(g) The predisposition or vulnerability model in which personality could facilitate the emergence of mental disorders and is, in fact, part of its etiopathogenesis. The vulnerability may be general, predisposing the person to a range of distress disorders, or be specific to a particular disorder (Blatt, 1974). High Neuroticism either causes the development of common mental disorders directly or enhances the impact of causal risk factors such as stressful life events.

It is proposed that personality traits may play a crucial role in the onset and development of PD (Clark, Watson, and Mineka, 1994), whereby extremes of personality traits indicate greater dysfunction in patients with anxiety disorders (Brandes et al., 2006). An anxious temperament and anxiety-related personality traits may represent intermediate phenotypes that predispose to PD (Na et al., 2011, de Ruiter, 1992). A strong relationship has been observed between high neuroticism and low positive emotions and PD (Bienvenu et al., 2001b; Bienvenu et al., 2004, Carrera et al., 2006, Zugliani et al., 2017). On the other hand, Introversion was found to be related to agoraphobia, but not to PD itself, while patients with agoraphobia tend to have higher Neuroticism, lower Extraversion or both (Bienvenu et al., 2001a; Bienvenu et al., 2004, Bienvenu et al., 2007). Other personality factors such as Openness, Agreeableness and Conscientiousness seem to be unrelated to PD (Bienvenu et al., 2001b, Enns and Cox, 1997, Carrera et al., 2006). The other reports indicate less Self-Directedness and Cooperativeness (Izci et al., 2014) and more obvious Harm Avoidance and fatigability (Izci et al., 2014; Kennedy et al., 2001; Wiborg et al., 2005) in patients with PD compared to healthy controls. In addition, PD patients show characteristics that are related to a developmental deficit in the capacity to regulate negative affect (Diamond, 1987). In particular, they tended to be shy and inhibited in childhood, especially showing a clear difficulty in expressing aggressiveness (Almeida and Nardi, 2002). The personality traits in PD could be influenced by gender and psychiatric comorbidity. Thus, it was shown that females with PD had higher Extraversion scores and were more fearful of physical consequences of anxiety than males, while males scored higher on angry hostility and depression facets of Neuroticism (Foot et al., 2004). Furthermore, Neuroticism as well as Agreeableness and Extraversion, though not Conscientiousness or Openness, significantly differed in PD patients with one disorder from those with two or more disorders (Cuijpers et al., 2005). Several other studies also showed an accentuation of certain personality traits, including Harm Avoidance, Neuroticism and Extraversion, in PD patients with affective comorbidity as compared to those with PD only (Ampollini et al., 1997; Bienvenu et al., 2001a; Bienvenu et al., 2001b; Freire et al., 2007, Zugliani et al., 2017). Neuroticism and Extraversion have also shown a strong correlation with the accumulation and severity of depression and agoraphobia with PD (Zugliani et al., 2017). Taken together, studies indicate significant alterations in the personality profiles of patients with PD, which are more pronounced when

comorbid with affective disorders. In terms of coexisting personality disorders, the high rates of cluster B (antisocial, borderline, histrionic, and narcissistic) and cluster C (avoidant, dependent, and obsessive-compulsive) personality disorders are reported in PD patients (Yates et el., 2009, Ozkan M, 2005; Skodol et al., 1995; Bienvenu et al., 2009; Bienveu, 2005, Grant, 2005). The stronger association was observed for borderline personality disorder (BPD, whereas 80% of in-patients with BPD met the criteria of anxiety disorders, including 48% having PD (Zanarini et al., 1998). Notably, that patients having PD with agoraphobia tend to have a higher prevalence of personality disorder diagnoses than those without agoraphobia (Reich, 1987; Iketani et al., 2002).

2.5. Personality and treatment outcome in panic disorder

Although personality traits and disorders are defined as highly stable behaviour patterns (Kipperet al., 2009), several authors have suggested that personality traits can be influenced by acute symptoms and by aging (Rocca et al., 2006, Corchs et al., 2008) or even change, in particular Neuroticism, under the effect of clinical intervention, pharmacotherapy or cognitive-behavioural therapy (Tang et al., 2009, Clark et al., 2003, Barlow et al., 2013).

It should be noted that in contrast to depression the association between personality characteristics and treatment outcome in anxiety disorders, including PD, is less investigated and understood (Bienvenu and Brandes, 2005). However, such a relationship seems to be bilateral where personality may modify response to treatment, but in turn the treatment can lead to certain changes in personality patterns. In particular, it has been shown that personality deviations may affect severity of the PD (Sokol et al., 1995, Ozkan et al., 2005), negatively influence treatment response (Slaap and den Boer 2001; Marchesi et al., 2006a) and contribute to a lesser decrease in specific panic and agoraphobic symptoms during a treatment course in comparison with PD without co-morbid personality disorders (Prasko et al., 2005). However, the evidence that personality disorders may worsen the prognosis of PD or lead to a longer treatment course (Prasko et al., 2005) is not supported by other observations (Hofmann et al., 1998). Controversial results have also been reported regarding the possible effect of personality traits on treatment outcome in PD. Therefore, Navarro et al. (2013) showed that borderline personality traits presenting in PD patients at the onset of the disease might worsen the response to pharmacological treatment. In some other studies, only the borderline traits have negatively influenced the remission of panic attacks following one-year treatment with SSRIs in PD patients, whereas the number of other personality traits did not affect the outcome of medication (Marchesi et al., 2006a; Hoffmann et al., 1998). In contrast, the borderline traits predicted a better treatment outcome at the six-month follow-up observation, whereas obsessive-compulsive personality traits were negatively related to treatment outcome (Dreessen et al., 1994). As was suggested, the effect of personality on treatment outcome in PD may depend on

several factors, including methodological variations across studies, differences in duration of follow-up, applied medications and definition of PD remission (Marchesi et al., 2006a). Earlier, Dreessen et al. (1998) reviewed 15 studies in aiming to evaluate the influence of personality disorders on treatment outcome in anxiety disorders, including PD. They concluded that the short-term treatment outcome (up to 3 months) of PD is not convincingly affected by the presence of categorical or dimensional personality disorder variables. Chavira et al. (2009) demonstrated that higher Neuroticism and higher anxiety sensitivity scores at baseline were associated with less probability of clinical improvement in 3 months in primary care patients with PD, which is in line with an earlier observation of Costa and McCrae (1985) from a 3-month follow-up study suggesting that lower Neuroticism scores at baseline predict better clinical improvement. Both prominent Neuroticism and higher harm avoidance seem to be the most important predictors of non-response to therapy with SSRIs, whereas higher Self-Directedness, Agreeableness and Cooperativeness predict a better response to drug treatment (Marchesi et al., 2006b). However, associations between basic personality dimensions and PD treatment response are not univocal. None of the explored personality traits as assessed by the Neuroticism-Extraversion-Openness Five-factor Personality Inventory was related either to clinical severity or to short-term response to SSRI treatment (Carrera et al., 2006), and no association between personality traits and PD symptom remission were found in other studies (Marchesi et al., 2006a).

In terms of the treatment effect on personality patterns in PD, some first reports have indicated that a large improvement in panic symptoms after anxiolytic medication with alprazolam or diazepam is accompanied by significant changes in neuroticism-related personality traits (Reich et al., 1991; Noyes et al., 1986). A positive influence on personality disorder characteristics in PD was also observed during both individual CBT and imipramine treatment; however, the efficacy was predicted by temperament (Hofmann et al., 1998). A more recent relatively small prospective study found that improvement in the symptoms of PD after 1year treatment with SSRIs was associated with the normalisation of paranoid traits and persistence of avoidant and dependent characteristics, suggesting that some personality traits in PD show, at least in part, a state phenomenon (Marchesi et al., 2005). In the later study by Marchesi et al. (2008,) higher levels of harm avoidance were found after 1 year of pharmacological therapy in patients with PD in remission compared to healthy controls. A recent study that used the SSP scale to evaluate the effect of 12-weeks of internet-based cognitive behaviour therapy on severe health anxiety has shown a significant reduction on neuroticism related scales, whereas traits relating to extraversion and aggression remained largely unchanged (Hedman et al., 2014). On the contrary, a significant decrease was observed in all anxiety-related scores as well as in the aggression and hostility-related scores on the Karolinska Scales of Personality (KSP) in PD patients after 6 months of treatment with SSRI citalopram (Neuger et al., 2002). Additionally, a significant decrease in the score on 8 of the 10 Minnesota Multiphasic Personality Inven-

tory scales was observed in PD patients following pharmacological treatment. However, the anxious and neurotic personality characteristics were still more pronounced in asymptomatic patients as compared to healthy controls (Kipper et al., 2009). Notably, although Brandes et al. (2006) revealed that remission from PD is generally associated with partial "normalization" of personality traits, some others assumed that personality traits remain stable over the course of PD (Morey et al., 2010, Santor et al., 1997).

3. RATIONALE FOR THE STUDIES

The relationship between personality and PD is still poorly understood and has become a topic of scientific debate and scrutiny. Considering that most of the studies cited above included relatively small samples and provided only preliminary or controversial evidences, further extensive investigations are warranted to evaluate the involvement of personality disposition in the course and treatment of PD. Furthermore, there is a vast number of studies that have sought to identify predictors of treatment response in anxiety disorders, including PD. Although, these studies have not as yet yielded findings that were robust enough to be clinically relevant, there is a strong belief that predictors of treatment response would contribute to the personalised medicine approach and, particularly, guide decision making in selection of the most suitable medication for individual patients. Moreover, similarly to other putative predictors, including demographic and clinical characteristics, personality traits are easy to evaluate and not as costly as genetic or neuroimaging biomarkers, which significantly facilitate the implementation of personality assessment in routine practice. In particular, a better understanding of the relationship between personality traits, a course of PD and its treatment outcome may significantly improve the prediction and management of this prevalent and highly disabling anxiety disorder. Furthermore, personality traits seem to play a crucial role in the pathogenesis and prognosis of all mental health disorders. Therefore, the further exploration of personality traits in patients with mental disorders, including PD, would have an important impact on fundamental knowledge about the development and course of these diseases. In particular, to achieve the goals of the current work, we chose the Swedish universities Scales of Personality (SSP) to measure the personality traits in PD patients. The SSP is a self-rated questionnaire based on the Karolinska Scales of Personality (KSP), an instrument designed to measure stable personality traits related to psychopathology (Schalling 1978; Gustavsson et al., 2000). The KSP scales tap personality traits that have biological correlates and could contribute to the development of mental disorders (Schalling et al., 1987; Klinteberg et al., 1987). Although the KSP does not aim to cover all aspects of personality, it characterises four fairly general temperament dimensions: anxiety, extraversion, socialisation and aggression (Schalling et al., 1987). During development of the SSP, some aggression and neuroticism-related scales of the KSP were dropped due to unsatisfactory psychometric properties. The final version of the SSP comprised 13 scales that demonstrated good psychometric properties in the Swedish normative sample (Gustavsson et al., 2000). Four scales of the SSP assess various aspects of vulnerability to anxiety. Another five scales reflect aggression and related traits. The remaining scales characterise sensation seeking, impulse control, relation to the social environment and conformity. Factor analysis suggests that the SSP scales measure three broader constructs: neuroticism, extraversion and aggressiveness (Gustavsson et al., 2000). The

SSP has shown to be useful as a personality measure in psychobiological research (Damberg et al., 2003, Jönsson et al., 2003). A widely accepted approach in the field of personality structure research is the five-factor model (Costa and McCrae1992b), which proposes that most individual differences in personality can be understood in terms of five basic dimensions. Relating the personality traits measured by the SSP with the five-factor model could give a better understanding of the position of these traits in the basic structure of personality. One of the standard instruments designed to measure these five factors and their facets is the Revised NEO Personality Inventory (NEO-PI-R). The NEO-PI-R has demonstrated a similar structure in various cultures (McCrae and Costa 1997). The SSP intends to measure temperament-like features, meaning that it also should be applicable in different social and cultural contexts. At the same time, the reliability and factor structure of the SSP in samples with different language and cultural backgrounds have not yet been studied. Thus, we aimed to test the reliability and validity of the Estonian version of the SSP. This also allows us to investigate the universality of the personality factors assessed by the SSP in a different social and cultural background. We also intend to characterise the position of SSP-measured traits within the basic personality dimensions of the five-factor model. Taken together, we found the SSP to be a promising instrument for its clinical exploitation in the evaluation of personality traits among patients with PD.

4. AIMS OF THE STUDIES

The general objective of the present work was to characterise the personality traits of patients with PD and to explore the relationship between personality disposition and treatment outcome in those patients by using validated SSP assessment. The specific aims were, as follows:

1. To test the reliability and validity of the Estonian version of the SSP (I)
2. To characterise the position of SSP-measured traits within the basic personality dimensions of the five-factor model (I)
3. To identify the differences in personality traits evaluated by SSP between patients with PD and healthy subjects (II)
4. To examine differences in personality dimensions between PD patients with and without affective comorbidity, and explore the relationship between SSP personality domains and various demographic and clinical variables of PD (II)
5. To examine the effect of escitalopram treatment on personality traits in PD patients (III)
6. To identify whether the treatment outcome of PD could be predicted by any personality trait as measured by using SSP (III)

5. MATERIALS AND METHODS

5.1. Subjects

A total of 529 subjects participated in the study I, among them 174 (32.9%) men and 355 (67.1%) women. The average age was 35.7 years (standard deviation, s=14.0 years, range 18–74). The study group was formed of two samples. Sample 1 consisted of 331 healthy volunteers (106 men, 225 women, average age 39.1, s=13.5) who participated in different research projects conducted at the Department of Psychiatry of the University of Tartu. The absence of psychiatric disorders in this sample was confirmed by the Mini International Neuropsychiatric Interview (M.I.N.I. 5.0.0; Sheehan et al., 1998). Sample 2 was a convenience sample comprising 198 subjects with various educational and social backgrounds (68 men, 130 women, average age 30.1 years, s=12.9). The sample consisted of university students, their acquaintances, relatives and workmates.

The study II sample consisted of 193 patients (45 men, 148 women, average age 36.9, s=12.3) with PD recruited at the Psychiatry Clinic of the Tartu University Hospital and 314 healthy subjects (94 men, 220 women, average age 38.9, s=13.8) recruited by newspaper advertisement in Tartu, Estonia. Diagnosis of PD according to DSM-IV criteria was verified using the Mini International Neuropsychiatric Interview (M.I.N.I. 5.0.0; Sheehan et al., 1998) and substantiated by psychiatric history and medical records. At the time of assessment, 126 of patients (65.3%) had current symptoms of PD and 67 were in remission. PD patients with current or past comorbidity with mood disorders or with other anxiety disorders were included in the study, but no other psychiatric comorbidity was allowed. Personality disorder was not assessed, it may be considered as limitation of the study. According to the clinical assessments 71 (36.8%) patients were defined as “PD only” group, who never met criteria for any other psychiatric diagnosis, with the exception of agoraphobia. The remaining 122 patients (63.2%) with comorbid mood or anxiety disorders were defined as “PD comorbid” group. Major depressive disorder was the most frequent comorbid or lifetime co-existing condition, which was diagnosed in 93 patients (with its current presence in 60 patients); whereas the criteria for bipolar disorder were met in 29 patients (with its current presence in 7). Other anxiety disorders, including social phobia and obsessive-compulsive disorder, were detected in 46 patients. Concurrent agoraphobia was present in 115 (59.6%) of the patients, among them 46 were from “PD only” and 69 from “PD comorbid” group. The earlier onset of PD with first panic attacks before age of 30 years was observed in 106 patients, whereas in 87 patients PD has developed in later lifetime period. The healthy subjects were interviewed using the M.I.N.I. and questioned about their family psychiatric history. Only those without personal or family (defined as first-degree relatives) history of psychiatric disorders were included in this study. The majority of the subjects were of Estonian ethnicity with a

similar between-group distribution (99% among patients and 95% among controls).

The study III sample consisted of 110 adult patients with PD. Participants were recruited at the Psychiatry Clinic Outpatient Department or through referral from the Emergency Department of the North Estonia Regional Hospital. Three patients were excluded (two by patient request, one lost to follow-up); therefore, 107 PD patients (mean age = 34, s = 11.7 years; 71 females) were included in the final sample of the study. The diagnosis of PD according to the DSM-IV criteria was verified using the Mini International Neuropsychiatric Interview and substantiated by psychiatric history and medical records. PD patients with current or past co-morbidity with mood disorders or with other anxiety disorders were allowed to take part in the study. However, other problems, such as schizophrenia or another psychotic disorder, severe suicide risk, substance abuse or dependence, organic mental disorder, severe personality disorder, serious unstable medical condition (i.e. endocrinological, liver, respiratory, cardiovascular diseases), were excluded. The majority of the subjects were of Estonian ethnicity (84.1%). All patients were unmedicated and did not receive any formal psychological help for at least 3 months before this trial and during the investigation.

5.2. Ethical considerations

The Human Studies Ethics Committee of the University of Tartu approved the study protocols, and all participants provided written informed consent.

5.3. Measures

5.3.1. The Mini International Neuropsychiatric Interview (M.I.N.I.5.0.0.)

Diagnosis of PD and psychiatric co-morbidity according to DSM-IV criteria was verified using the Mini International Neuropsychiatric Interview (M.I.N.I.5.0.0.; Sheehan et al., 1998) and substained by psychiatric history and medical records (II, III). The Mini International Neuropsychiatric Interview (M.I.N.I.) is a structured diagnostic interview, developed for DSM-IV and ICD-10 psychiatric disorders. In 1999 M.I.N.I. 5.0.0. was adapted to Estonian at the Department of Psychiatry of Tartu, University of Tartu (Shlik et al.,1999). The absence of psychiatric disorders in sample of healthy subjects in control group (I, II) was confirmed by the M.I.N.I.5.0.0.; also subjects were questioned about their family psychiatric history (II).

5.3.2. Swedish universities Scales of Personality (SSP)

The Swedish universities Scales of Personality (SSP) is a self-rated questionnaire based on the Karolinska Scales of Personality (KSP) designed to measure stable personality traits related to psychopathology (Gustavsson et al., 2000). The SSP comprises of 91 items grouped into 13 scales: Somatic Trait Anxiety (STA), Psychic Trait Anxiety (PsTA), Stress Susceptibility (SS), Lack of Assertiveness (LA), Impulsiveness (I), Adventure Seeking (AS), Detachment (D), Social Desirability (SD), Embitterment (Em), Trait Irritability (TI), Mistrust (M), Verbal Trait Agression (VTA), and Physical Trait Aggression (PHTA). Each scale is formed by 7 items rated on a scale of 1 = does not apply at all, to 4 = applies completely.

The factor analysis of the original SSP yielded three factors: neuroticism, aggressiveness and extraversion (Gustavsson et al., 2000).

The raw scores were converted into T-scores using the raw score means and standard deviations of men and women from Estonian normative sample in study I. Only T-scores were used in the analysis in studies II and III.

All participants self-evaluated their personality traits using the Estonian version of SSP (I, II, III) (Aluoja et al., 2009).

(I) The SSP was completed by all participants of the study (both samples).

(II) At the time of assessment all the patients (with current symptoms of PD and in remission) and all the control subjects completed the Estonian version of SSP to evaluate their personality traits.

(III) The Estonian version of SSP was completed by study group twice, at the beginning of the study and at the last visit after 12-week treatment with SSRI escitalopram.

5.3.3. The revised NEO Personality Inventory (NEO-PI-R).

The NEO-PI-R is a 240-item self-report questionnaire that measures personality structure according to the five-factor model (Costa&McRae, 1992b). Similarly to the original, the Estonian version of the NEO-PI-R (Kallasmaa et al., 2000) provides scores on the five personality dimensions: Neuroticism (N), Extraversion (E), Openness (O), Agreeableness (A), and Conscientiousness (C). Each personality domain is composed of six facet scales. Responses are made on a five-point Likert-type scale (from strongly agree to strongly disagree). One of the standard instruments designed to measure these five factors and their facets is the Revised NEO Personality Inventory (NEO-PI-R) (Costa et al., 1992). NEO-PI-R has demonstrated similar structure in various cultures (McCrae& Costa 1997). In study I 197 subjects from the Sample 2 completed Estonian version of the NEO-PI-R.

5.3.4. Panic Disorder Severity Scale (PDSS)

The PDSS (Shear et al., 1997) is used for assessment of clinical severity and treatment response of PD. The PDSS is seven-item measure, score range 0–28, comprised of five items assessing core DSM-IV symptoms of PD, with or without agoraphobia, and two items rating work and social impairment (Shear et al., 1997). The scale has been considered sensitive to change with medication treatment (Pollack et al., 1998). The scale has been translated into several languages and findings strongly support the reliability and validity of the PDSS in different cultural background (Shear et al., 2001, Lee et al., 2009, Barlow et al., 2000). For screening of patients a cut-off score 8 was recommended, which identifies patients with current PD with a sensitivity of 83.3% and a specificity of 64% (Shear et al., 2001). The PDSS score 7 or less has been used in several studies for defining of remission (Furukawa et al., 2009, Shear et al., 2001, Park et al., 2012, Seki et al., 2016) and is considered the point of remission in this study. All patients in the study III were assessed using the PDSS beginning from the baseline up to the endpoint of the study in every two weeks.

5.3.5. The Clinical Global Impression scale (CGI)

The Clinical Global Impression scale (Guy, 1976) is a 3-item observer-rated scale commonly used to measure symptom severity, global improvement, and therapeutic response. Each component of the CGI is rated separately. The Clinical Global Impression – Severity scale (CGI-S) is a 7-point scale to rate the severity of patient illness at the time of assessment, relative to the clinician's past experience with patients who have the same diagnosis. Considering total clinical experience, a patient is assessed on severity of mental illness at the time of rating 1, normal, not at all ill up to 7, extremely ill.

The Clinical Global Impression – Improvement scale (CGI-I) is a 7 point scale for assessment how much the patient's illness has improved or worsened relative to a baseline state at the beginning of the intervention and rated as: 1, very much improved; 2, much improved; 3, minimally improved; 4, no change; 5, minimally worse; 6, much worse; or 7, very much worse.

The Clinical Global Impression – Efficacy Index is a 4 point × 4 point rating scale that assesses the therapeutic effect of the treatment as 1, unchanged to worse; 2, minimal; 3, moderate; 4, marked by side effects rated as none, do not significantly interfere with patient's functioning, significantly interferes with patient's functioning and outweighs therapeutic effect. With this scale therapeutic efficacy and treatment-related adverse events should be taken into account. Clinical severity and treatment response in the study III were assessed using the CGI, every two weeks during the study.

5.3.6. Hamilton Anxiety Scale (HAM-A)

Hamilton Anxiety Scale (HAM-A) (Hamilton, 1959) was developed to measure the severity of anxiety symptoms and is widely used in clinical and research settings. The HAM-A is an interview-based scale, consists of 14 items, each defined by a series of symptoms, and measures psychic anxiety (mental agitation and psychological distress) and somatic anxiety (physical complaints related to anxiety). Each item is simply given a 5-point score – 0 (not present) to 4 (severe). HAM-A was used as a secondary scale in the study III for clinical assessments, every two weeks during the study.

5.3.7. Toronto Side-effect Scale (TSES)

Toronto Side-effect Scale (TSET) is a 32-item instrument used to evaluate possible adverse events, incidence, frequency, and severity of central nervous system, gastrointestinal, and sexual side effects (Vanderkooy et al., 2002). TSES was used as a secondary scale for clinical assessments in the study III, every two weeks during the study.

5.3.8. The Emotional State Questionnaire (EST-Q)

The Emotional State Questionnaire (EST-Q) (Aluoja et al., 1999) is a self-rated questionnaire, constructed on the basis of the relevant diagnostic criteria in the DSM-IV (APA, 1994) and the 10th revision of the International Classification of Diseases and Related Health Problems (ICD-10, World Health Organization 1993). The EST-Q contains 28 questions in five subscales; items are rated on a 5-point frequency scale ranging from 0 (never) to 4 (continuously).

5.3.9. Sociodemographic measures

Data on sex, gender, age, years of education, employment, smoking habit, alcohol drinking frequency, presence of somatic co-morbidities and marital status were recorded in the study groups according to the study design (I, II, III) from the structured interviews.

5.4. Treatment

The patients in the study III were treated with 10–20 mg/day of escitalopram for 12 weeks using an open-label placebo non-controlled study design. No other medications were permitted during the treatment period, except for hormonal contraceptives. Additionally, zolpidem or zopiclon for insomnia and alprazolam

for acute anxiety or panic symptoms were also allowed during the first 6 weeks. All patients started the treatment with a dose of 10 mg/day of escitalopram for the first 4 weeks. The patients who showed at least a 50% decline in the PDSS total score at week 4 continued taking 10 mg of escitalopram until the end of the study. The dose of escitalopram was increased and maintained at 20 mg in patients who demonstrated less than a 50% decrease in PDSS total score at week 4. At the end of week 12, remission was defined as a patient who meets all three criteria – the score on the CGI improvement scale 2 or less, the PDSS score 7 or less – the cut-off point, used in several studies for defining of remission, and no panic attacks for at least the last 2 weeks. Patients who did not meet these criteria were defined as non-remitters. The severity of the panic symptoms and treatment response were rated by a psychiatrist (UV), who was blind to the personality trait measures. During each visit, the patients were also asked to report on their regularity of taking the medication. Adherence to medication was good – by patients self-report none of the patients had more than 3 days drug holiday.

5.5. Statistical analysis

The data were analyzed using the software package STATISTICA 8 (StatSoft Inc., Tulsa, OK, USA) and statistical software R 3.1.1. (R Core Team, 2014). In the study I the internal consistency of the SSP scales was assessed by calculating Cronbach's α coefficients. To evaluate the factorial validity of the SSP a principal component analysis with a varimax rotation was conducted on the scales. The factors were extracted on the basis of an eigenvalue greater than one. In subsample 2 the external validity of the SSP was evaluated by calculating Pearson product moment correlations between the SSP scales and the NEO-PI-R scales. Correlations between the SSP and NEO-PI-R scale facets were reported only if they provided additional information for understanding of the SSP scales. Student's t-test was used to evaluate sex differences. In the study II the non-parametric tests, including Chi-squared, Fisher's exact test and Mann-Whitney U-test, were used as appropriate. Correlations were estimated with Pearson product-moment correlation analysis. Multiple logistic regressions were used to analyze the relative influence of personality variables. Only variables which showed a significant relationship with PD in univariate analyses were entered into multivariate models. Three broader factors, neuroticism, extraversion and aggressiveness, were included in our analysis. The comparisons of SSP subscales and factors were performed for all patients and separately for subgroups of those with and without comorbidity. The comparisons of SSP traits and factors were also done in patient subgroups divided according to predefined clinical phenotypes (current PD versus remission status, presence or absence of agoraphobia, early or late onset of PD, presence or absence of family psychiatric history). The results of between-group comparisons of SSP scores were considered nominally significant at $p<0.05$ level with a conservative

estimation of significance after Bonferroni correction for multiple comparisons on 13 SSP traits at $p<0.00384$ level. In the study III baseline and final SSP sub-scales were described by mean, minimum and maximum, Wilcoxon signed rank test was used to test the significance of the change between the end and baseline scores of the study. The association between the baseline scores of SSP sub-scales and the changes of PDSS, CGI-S, HAM-A and EST-Q depression was evaluated using partial correlation coefficients with 95% confidence intervals (CI). Similarly, the association between changes in the scores of SSP sub-scales and changes of PDSS, CGI-S, HAM-A and EST-Q depression was evaluated using partial correlation coefficients with 95% CI. The association between the baseline scores of SSP sub-scales and the probability of good treatment response (final PDSS≤7) was analysed by binary logistic regression resulting in odds ratios (OR) with 95% CI. All of the analyses of associations were adjusted for sex, age, years of education, level of drinking frequency, presence of somatic co-morbidities and for the presence of mild depression and/or agoraphobia. The resulting *p*-values were considered nominally significant at $p<0.05$ level; the Holm-Bonferroni correction for multiple comparisons was used. Regression assumptions were checked by graphical methods, where applicable.

6. RESULTS AND DISCUSSION

6.1. Study I: Factor structure of the Swedish universities Scales of Personality and position within the five-factor model in an Estonian sample

6.1.1. The gender differences for the SSP

Mean values of the SSP for the whole study sample and separately for males and females are presented in Table 1. Females scored significantly higher on Psychic Anxiety, Stress Susceptibility, Lack of Assertiveness, and Social Desirability. Men scored higher on Verbal and Physical Aggression, Mistrust, and Adventure Seeking. The highest gender differences emerged for Aggression and Anxiety scales. Internal consistency coefficients for the SSP scales ranged from 0.58 (Detachment) to 0.85 (Trait Irritability).

Table 1. Means, standard deviations, Cronbach alphas, and gender differences for the SSP scales

SSP scales	Total			Men		Women		t
	Mean	s	(α)	Mean	s	Mean	s	
Somatic Trait Anxiety	1.84	0.54	0.75	1.82	0.52	1.84	0.55	0.39
Psychic Trait Anxiety	2.17	0.59	0.82	2.03	0.56	2.24	0.60	4.00‡
Stress Susceptibility	2.17	0.50	0.73	2.11	0.50	2.20	0.49	1.97*
Lack of Assertiveness	2.35	0.48	0.64	2.28	0.48	2.39	0.48	2.64†
Impulsiveness	2.42	0.45	0.62	2.42	0.43	2.42	0.46	0.17
Adventure Seeking	2.63	0.56	0.80	2.71	0.55	2.59	0.56	–2.21*
Detachment	2.23	0.44	0.58	2.27	0.44	2.21	0.44	–1.62
Social Desirability	3.05	0.41	0.66	2.95	0.39	3.09	0.41	3.81‡
Embitterment	1.99	0.49	0.73	2.00	0.51	1.99	0.48	–0.30
Trait Irritability	2.30	0.61	0.85	2.33	0.58	2.28	0.63	–0.99
Mistrust	2.11	0.50	0.76	2.21	0.49	2.06	0.49	–3.34†
Verbal Trait Aggression	2.32	0.59	0.78	2.51	0.57	2.23	0.57	–5.45‡
Physical Trait Aggression	2.10	0.62	0.84	2.44	0.60	1.93	0.57	–9.54‡

* $p<0.05$, † $p<0.01$, ‡ $p<0.001$; *Means and standard deviations are presented as raw scores.*

6.1.2. The principal component analysis of the SSP scales

Present study yielded three factors in analysis of the SSP scales, with an eigenvalue greater than unity, accounting for 62.9% of the total variance (Table 2). The first factor grouped scales that characterise neuroticism, accounting for 27.8% of the variance. Both forms of Trait Anxiety (somatic and psychic), Stress Susceptibility, Lack of Assertiveness, and Embitterment had highest loadings on this factor. The second factor accounted for 20.2% of the variance and included Verbal and Physical Trait Aggression, Trait Irritability, Detachment, and low Social Desirability, thus indicating aggression and nonconformity. Although Detachment and Trait Irritability had highest loadings on the second factor, they also loaded somewhat on the third and the first factors. The third factor comprised Impulsiveness and Adventure Seeking, accounting for 14.8% of the variance. Mistrust loaded nearly equally on two factors, relating to neuroticism and aggression.

Table 2. Results of the principal component analysis with a varimax rotation of the SSP scales

Scales	Factor 1*	Factor 2*	Factor 3*
Somatic Trait Anxiety	**0.68**	0.26	0.29
Psychic Trait Anxiety	**0.89**	0.08	0.01
Stress Susceptibility	**0.76**	0.25	–0.03
Lack of Assertiveness	**0.80**	–0.14	–0.09
Impulsiveness	0.20	0.22	**0.75**
Adventure Seeking	–0.03	0.07	**0.79**
Detachment	0.38	**0.50**	–0.40
Social Desirability	–0.14	**–0.70**	0.04
Embitterment	**0.65**	0.31	0.20
Trait Irritability	0.49	**0.58**	0.36
Mistrust	**0.51**	**0.50**	0.01
Verbal Trait Aggression	0.05	**0.72**	0.47
Physical Trait Aggression	0.03	**0.70**	0.29

* Items defining the factors are boldfaced

6.1.3. The correlations between the SSP and NEO-PI-R scales

The correlations between the SSP scales and the five dimensions of personality assessed by the Estonian NEO-PI-R are shown in Table 3. Due to the large number of correlations performed, Bonferroni adjusted alpha of $p<0.001$ was applied to correlation coefficients. NEO-PI-R domain Neuroticism correlated mainly with SSP neuroticism factor scales. The strongest relationships were found with Psychic Trait Anxiety and Stress Susceptibility. Extraversion related

positively to Adventure Seeking and Impulsiveness, and negatively to Detachment, Psychic Anxiety, Lack of Assertiveness, Stress Susceptibility, and Mistrust. Agreeableness correlated positively with SSP Social Desirability and negatively to Aggression-Irritability scales, Mistrust, and Embitterment. NEO-PI-R dimensions Openness and Conscientiousness had somewhat weaker correlations with the SSP. Conscientiousness related highest to Social Desirability, and Openness to Adventure Seeking. Two SSP scales, Impulsiveness and Physical Trait Aggression had only one moderate correlation with NEO-PI-R domains. To get a better understanding of the relationships of SSP scales with five factors we also looked at the correlations with NEO-PI-R facet scales. SSP Impulsiveness correlated positively with Neuroticism facets Impulsiveness (r=0.44) and Hostility (r=0.32), Extraversion facets Assertiveness (r=0.29), Activity (r=0.24), Excitement-Seeking (r=0.31), and Positive Emotions (r=0.29), and negatively with Agreeableness facets Compliance (r=0.32) and Modesty (r=–0.31). The highest negative correlation emerged between Impulsiveness and Deliberation (r=–0.54), which is a facet of Conscientiousness. SSP Physical Trait Aggression correlated positively with Neuroticism facet Hostility (r=0.34), and negatively with Agreeableness facets Trust (r=–0.25), Straightforwardness (r=–0.34), and Compliance (r=–0.54).

Table 3. Correlations between the SSP and the NEO-PI-R scales in sample 2 (n=197)

	N	E	O	A	C
Somatic Trait Anxiety	0.61*	–0.20	–0.12	–0.24	–0.23
Psychic Trait Anxiety	0.76*	–0.48*	–0.25*	–0.04	–0.23
Stress Susceptibility	0.67*	–0.44*	–0.19	–0.10	–0.38*
Lack of Assertiveness	0.44*	–0.45*	–0.27*	0.19	–0.17
Impulsiveness	0.13	0.35*	0.10	–0.19	–0.19
Adventure Seeking	–0.03	0.53*	0.32*	–0.16	–0.02
Detachment	0.30*	–0.67*	–0.35*	–0.20	–0.13
Social Desirability	–0.35*	0.21	0.02	0.52*	0.46*
Embitterment	0.65*	–0.22	–0.23	–0.32*	–0.35*
Trait Irritability	0.55*	–0.12	–0.08	–0.50*	–0.28*
Mistrust	0.48*	–0.36*	–0.26*	–0.43*	–0.18
Verbal Trait Aggression	0.27*	0.10	0.15	–0.60*	–0.27*
Physical Trait Aggression	0.16	0.02	–0.06	–0.44*	–0.07

* $p<0.001$

6.1.4. Discussion

The aim of this study was to test the reliability and validity of the Estonian version of the SSP in order to use the scales in further studies of the role of personality factors in mental disorders. Thus, we evaluated the Estonian SSP in

reference to the Swedish original data, and we characterised the position of the SSP-measured traits within the basic personality dimensions of the five-factor model. The internal consistency of the Estonian SSP scales was in an acceptable range and resembled the Swedish normative data (Gustavsson et al., 2000). The range of the Cronbach α coefficients was between 0.59 and 0.84 in the Swedish study, while they ranged from 0.58 to 0.85 in the Estonian sample. The internal consistency of the anxiety and aggression scales was good and comparable with the original sample. Only two scales, Detachment and Impulsivity, had somewhat low internal consistency. General trends in sex differences were similar in the Estonian and Swedish samples: women scored higher on neuroticism-related scales and men on aggression scales. The one exception was not finding gender differences in the Detachment scale, while in Swedish KSP and SSP studies men have consistently scored higher on detachment than women (Gustavsson et al., 2000; Gustavsson 1997).

The Estonian data revealed a similar three-factor structure of the SSP that was found in the Swedish sample. The Neuroticism factor was identical in the two studies. This finding is important, as clinical researches have identified neuroticism as one of the key contributors to psychopathology (Lahey, 2009). Although the SSP was constructed more for the assessment of psychopathology and the NEO-PI-R for normative personality, both contain Neuroticism factors that are strongly correlated. This also confirms the universality of the general Trait of Neuroticism.

We found analogous factors to Aggression and Extraversion of the Swedish sample (Gustavsson et al., 2000), except for Detachment scale, which according to the Swedish data loaded negatively into the extraversion factor but in our study was closer to aggression. An ambiguous nature of Detachment scale has been earlier observed in factor-analytical studies of the KSP. Some studies indicated that Detachment was a sign of low sociability and thus related to Extraversion (Schalling et al., 1987, Zuckerman et al., 1991), whereas other studies showed its relatedness to Irritability, low Social Desirability and Suspicion (Gustavsson et al., 1997; Ortet et al., 2002). These results probably reflect the complex nature of the construct of Detachment, which is a tendency to avoid close contacts but is also related to the perception of others as being hurtful or untrustworthy (Bornstein et al., 2003). The latter aspect is related to an affective-cognitive side of aggression (irritability and hostility), but not necessarily to its behavioural component represented by Verbal and Physical Aggression scales of the SSP. It is of interest that Detachment and Irritability may even have some common biological correlates (Stalenheim, 2004).

The Neuroticism factor of the SSP is represented in major models of personality (Costa and McCrae, 1992b, Eysenck and Eysenck 1985). The same holds for the second SSP factor that was earlier conceptualised as Extraversion, and combines Adventure Seeking with Impulsiveness (Gustavsson, 2000, Schalling et al., 1987). The third SSP factor, Aggression, joins tendencies to act aggressively with irritability and unfriendly attitudes, and thus resembles Eysenck's Psychoticism (Eysenck and Eysenck 1976). This is in line with other

studies confirming that readiness to express aggression and hostile attitudes form a separate personality dimension (Zuckerman et al., 1991; Zuckerman et al., 1993).

The relationships of the SSP factors with basic personality dimensions were also confirmed by the correlations with the NEO-PI-R scales. Overall, the relationships with the five-factor model were in the expected direction. Scales belonging to the SSP Neuroticism factor had the strongest correlations with the NEO-PI-R Neuroticism scale, confirming that they assess a tendency to experience negative emotions, especially anxiety. Impulsiveness and Adventure Seeking were joined in the same factor and had somewhat similar correlates of NEO-PI dimensions. Both were related to Extraversion but Adventure Seeking was also connected to Openness. This suggests that the need for change and action is related to curiosity and openness to ideas. It has been demonstrated that NEO-PI Openness is related to sensation seeking (García et al., 2005), which is analogous to the SSP Adventure Seeking. The SSP Impulsiveness deserves closer inspection. Impulsivity is a construct that has been positioned differently in the structure of personality. In the five-factor model, it has been placed in the Neuroticism domain (Costa and McCrae, 1992b), while Zuckerman et al. (1991) considered Impulsiveness the closest to sensation seeking and distinct from Neuroticism. Our results show that the SSP Impulsiveness had the strongest association with the low Deliberation of Conscientiousness domain. Similarly, a previous study of health-related personality traits found a relationship between the SSP Impulsiveness items and the Conscientiousness construct (Gustavsson et al., 2003). This indicates that from several aspects of impulsivity, the SSP Impulsiveness measures a lack of premeditation, i.e. a tendency to act on the spur of the moment and without considering the consequences. Like the SSP, most existing impulsivity measures assess lack of premeditation, which has been associated with NEO-PI-R low Deliberation (Whiteside and Lynam, 2001). This aspect of impulsivity is also related to several forms of psychopathology and is closest to Dickman's concept of dysfunctional impulsivity (Dickman, 1990). These results might give a new perspective to the SSP factor combining Impulsiveness with Adventure Seeking. Often in KSP and SSP studies, this factor has been regarded as reflecting the extraversion construct (Gustavsson et al., 2000; Schalling et al., 1987), but present results suggest that the psychological core of it could be a lack of constraint or disinhibition rather than sociability and energy. Clark and Watson (Clark and Watson, 1999) have argued that disinhibition versus constraint is the third general temperament factor besides negative emotionality/neuroticism and positive emotionality/extraversion. Further studies are needed to confirm whether the combination of non-planning impulsivity and adventurousness reflects extraversion or disinhibition, but the latter could be in better agreement with the aim of the SSP in assessing traits constituting vulnerability to psychiatric disorders.

The SSP aggression scales are associated with the NEO-PI-R low Agreeableness and high Neuroticism. In the five-factor model, aggression belongs to

several dimensions, such as Neuroticism that contains the Angry hostility facet, and Agreeableness, concerning the Compliance facet in particular (Costa and McCrae, 1992). Our results are in accordance with Martin et al. (2000) showing that the behavioural, affective and cognitive components of aggression have different NEO-PI-R correlates. Our study supports the idea that the tendency towards aggressiveness constitutes a separate general personality dimension. At least when considering personality traits related to psychopathology, it seems appropriate to treat aggressiveness as a separate construct. Overall, the relationships between the NEO-PI-R and the SSP confirm the validity of the latter instrument. The discrepancies between the two instruments may result from the fact that the SSP has more specific orientation than the NEO-PI-R. While SSP tries to capture nuances of character pathology, such as different types of aggression and anxiety, the NEO-PI-R aims to give a comprehensive assessment of normal personality traits.

A limitation of the study should be addressed. Our study did not include randomly selected population sample like the Swedish study, but instead consisted of healthy research volunteers and a convenience sample. It has been argued that volunteers in research projects cannot be considered a normative sample because of the high rate of psychopathology among them (Shtasel et al., 1991). We tried to correct that possible bias by using a structured diagnostic psychiatric interview (MINI) to rule out mental disorders in the sample of volunteers.

6.2. Study II: Evaluation of personality traits in PD using SSP

6.2.1. Demographic and clinical characteristics

There were no significant differences between patient and control groups in age and sex distribution or in other demographic characteristics, including educational level, marriage and occupational status, however more smoked cigarettes per day were reported by patients as compared to controls (Table 4). None of demographic variables significantly differed between “PD only” and “PD comorbid” groups. Both patient groups had similar mean age of onset of PD (p=0.49) and similar proportions of those with or without agoraphobia (p=0.26), with current panic symptoms or in remission (p=0.67) or of those with or without somatic comorbidity (p=0.50). However patients with comorbid PD had a higher load of family history of psychiatric disorders than “PD only” group (51.3% vs. 33.8%, respectively; p=0.019), and more smokers were found in comorbid PD group than in pure PD (41.8% vs. 26.8%, p=0.036).

Table 4. Demographic characteristics of patient and control groups

Characteristics	PD patients	Healthy subjects	Statistics
Females	148 (76.7%)	220 (70.1%)	
Males	45 (23.3%)	94 (29.9%)	χ^2=2.63, p=0.11
Mean age	36.9±12.3	38.9±13.8	F=2.83; p=0.09
Education	13.8±2.9	14.1±2.9	F=1.29; p=0.26
Married or common-law	130 (67.4%)	209 (66.6%)	χ^2=0.03, p=0.85
Employed or student	146 (75.7%)	249 (79.3%)	χ^2=0.93, p=0.34
Smokers	70 (36.3%)	109 (34.7%)	χ^2=0.13, p=0.72
Cigarettes per day	5.4±8.2	3.7±6.6	F=5.63; p=0.02

6.2.2. Personality differences between total PD group and healthy controls

The analysis of SSP assessments revealed robust differences in personality traits between patients with PD and healthy controls (Table 5). All traits, except for Detachment and Physical Trait Aggression, were significantly deviated in PD group, with the scores for Adventure Seeking and Social Desirability being lower, and all the others being higher in patient group. The SSP factors of Neuroticism and Aggressiveness, but not Extraversion, were significantly higher in PD group than in controls (Table 5). In multivariate logistic regression analyses, Somatic Trait Anxiety, Stress Susceptibility, Lack of Assertiveness and Adventure Seeking remained significant predictors of PD (Table 6).

Table 5. SSP personality characteristics in PD and control groups

SSP traits	PD all (n=193)	PD only (n=71)	PD comorbid (n=122)	Control (n=314)	PD all vs. Control	PD only vs. Control	PD comorbid vs. Control	PD comorbid vs. PD only
Somatic Trait Anxiety	66.8±11.2	63.0±9.8	68.9±11.4	46.6±8.4	**<0.000001**	**<0.000001**	**<0.000001**	**0.000249**
Psychic Trait Anxiety	60.3±10.8	56.8±11.3	62.4±10.0	47.6±9.6	**<0.000001**	**<0.000001**	**<0.000001**	**0.000892**
Stress Susceptibility	60.8±10.9	56.7±10.0	63.1±10.7	47.6±9.6	**<0.000001**	**<0.000001**	**<0.000001**	**0.000128**
Lack of Assertiveness	55.1±11.5	53.2±11.8	56.1±11.2	48.7±9.9	**<0.000001**	0.004	**<0.000001**	0.087
Impulsiveness	51.0±10.4	50.3±11.1	51.5±10.1	48.2±9.8	**0.003**	0.219	**0.002**	0.309
Adventure Seeking	45.7±10.1	44.9±9.6	46.2±10.3	48.6±10.2	**0.002**	0.004	0.034	0.352
Detachment	52.0±9.7	49.9±10.3	53.3±9.2	49.5±9.1	0.007	0.810	**0.000132**	0.005
Social desirability	47.4±9.5	47.9±8.8	47.1±10.0	51.9±9.9	**0.000001**	**0.001**	**0.000008**	0.508
Embitterment	57.0±11.1	52.2±9.5	59.8±11.0	48.8±9.7	**<0.000001**	0.008	**<0.000001**	**0.000002**
Trait Irritability	57.5±9.8	54.4±9.5	59.4±9.5	46.9±9.3	**<0.000001**	**<0.000001**	**<0.000001**	**0.0001**
Mistrust	53.4±12.0	50.8±10.3	54.8±12.7	48.7±9.5	**0.000012**	0.068	**0.000003**	0.067
Verbal Trait Aggression	51.0±9.8	49.4±10.1	51.9±9.6	47.2±9.1	**0.000038**	0.112	**0.000009**	0.100
Physical Trait Aggression	50.8±11.0	50.2±11.6	51.2±10.6	47.9±9.5	0.006	0.301	**0.003070**	0.255
SSP factors								
Neuroticism	60.0±8.9	56.4±8.2	62.1±8.6	47.9±7.3	**<0.000001**	**<0.000001**	**<0.000001**	**<0.000001**
Extraversion	48.4±8.7	47.6±9.3	48.9±8.4	48.4±8.5	0.935	0.323	0.550	0.188
Aggressiveness	53.0±7.5	51.5±7.2	53.9±7.6	47.5±7.0	**<0.000001**	**0.0001**	**<0.000001**	0.034

Bold *p*-values: the Bonferroni adjusted *p*-value corrected for multiple comparisons on 13 SSP traits at the $p<0.004$ level.

Table 6. Multivariate logistic regression analyses for PD (versus control group)

SSP traits	Total PD group				PD only				PD comorbid			
	B	OR	95%CI	*p*	B	OR	95%CI	*p*	B	OR	95%CI	*p*
Somatic Trait Anxiety	0.18	1.20	1.16–1.25	0.0001	0.19	1.20	1.15–1.26	0.000	0.17	1.19	1.14–1.25	0.000 1
Psychic Trait Anxiety	0.02	1.02	0.97–1.07	0.419	–0.04	0.97	0.92–1.01	0.160	0.05	1.05	0.98–1.12	0.143
Stress Susceptibility	0.05	1.05	1.01–1.10	0.013	0.03	1.03	0.98–1.08	0.296	0.06	1.06	1.01–1.12	0.022
Lack of Assertiveness	–0.06	0.94	0.90–0.98	0.003					–0.06	0.94	0.90–0.99	0.014
Impulsiveness	–0.01	0.99	0.95–1.03	0.597					–0.03	0.98	0.93–1.02	0.257
Adventure Seeking	–0.04	0.96	0.93–0.99	0.021								
Detachment									–0.02	0.98	0.94–1.03	0.484
Social Desirability	–0.02	0.98	0.95–1.01	0.208	–0.04	0.97	0.93–1.00	0.081	–0.02	0.98	0.94–1.03	0.399
Embitterment	–0.04	0.96	0.93–1.00	0.069					–0.01	0.99	0.94–1.04	0.686
Trait Irritability	0.03	1.03	0.99–1.09	0.183	0.00	1.00	0.95–1.04	0.867	0.05	1.05	0.99–1.12	0.093
Mistrust	–0.02	0.98	0.95–1.02	0.292					–0.04	0.96	0.92–1.00	0.070
Verbal Trait Aggression	–0.00	0.99	0.96–1.04	0.95					0.00	1.00	0.95–1.06	0.943
Physical Trait Aggression									–0.03	0.97	0.93–1.02	0.204

OR= odds ratio, 95%CI= 95% confidence intervals

6.2.3. Personality traits in patients with pure and comorbid PD

Comparison of comorbid PD and healthy controls showed significant differences in all SSP traits, except of Adventure Seeking; all traits, apart from Social Desirability with lower scores, were more expressed in comorbid PD group. Neuroticism and Aggressiveness, but not Extraversion showed significant differences between the groups (Table 5). Multivariate regression analyses in PD comorbid group showed significant differences remaining for Somatic Trait Anxiety, Stress Susceptibility and Lack of Assertiveness (Table 6). Patients with pure PD were characterized by increased anxiety-related traits, Stress Susceptibility, Irritability, and lower Social Desirability, whereas the scores for other traits did not significantly differ from those in controls. Additionally, the patients with PD only, demonstrated higher Neuroticism and Aggressiveness, but similar Extraversion, as compared to healthy subjects (Table 5). In multivariate analyses only Somatic Trait Anxiety remained significant for the group of PD only (Table 6). The comparison of the two PD groups showed that Anxiety Traits, Stress Susceptibility, Embitterment and Irritability were significantly more pronounced in patients with comorbid PD than in those with PD only, with no significant differences in other SSP traits. In respect to SSP factors, only Neuroticism significantly differed between these two PD groups (Table 5).

6.2.4. Associations of clinical and demographic factors with the personality

The patients with current PD had significantly higher scores for anxiety traits and Stress Susceptibility, but not for any other SSP traits, than PD patients in remission. Accordingly, only Neuroticism was significantly higher in patients with current PD (p=0.0002) as compared to the remitters. Patients with current PD showed significant differences from healthy controls on several SSP subscales, except Impulsiveness, Detachment and Physical Trait Aggression. On the other hand, patients with PD in remission reported six SSP subscales as similar to controls, including the same three as the patients with current PD, plus Lack of Assertiveness, Adventure Seeking and Mistrust. Nevertheless, both remitters and currently symptomatic patients demonstrated significantly higher Neuroticism and Aggressiveness as compared to healthy subjects (data are not shown). Comparisons of patients with earlier and later onset of PD or patients with and without family history of psychiatric disorders showed no significant differences on any SSP subscales or factors (data are not shown). Only Trait Irritability was significantly higher in PD with agoraphobia as compared to PD without agoraphobia (p=0.0028). In pure PD group no significant differences in SSP traits emerged between patients with and without agoraphobia. Although all three SSP factors showed higher scores in PD with agoraphobia, only Aggressiveness withstood Bonferroni correction (p=0.02 for Neuroticism, p=0.04 for Extraversion and p=0.0028 for Aggressiveness). SSP scores in PD group were not associated with gender, somatic morbidity, marital or occupational status (data are not shown).

6.2.5. Correlation data

The correlations between individual SSP traits and four variables, including age, onset of PD, education and number of smoked cigarettes per day, were examined in PD group. The analyses revealed modest, but significant correlations between age of patients and social desirability (r=0.18; *p*=0.01), onset of PD and Verbal Trait Aggression (r=–0.19; *p*=0.01), educational level and Embitterment (r=–0.20; *p*=0.006) and Mistrust (r=–0.21; *p*=0.005), and between smoking and Somatic Trait Anxiety (r=0.16; *p*=0.03) and Physical Trait Aggression (r=0.17; *p*=0.025). In addition, several correlations were observed for SSP factors (Table 4). In particular, Neuroticism was negatively correlated with years of education in PD group and in all studied subjects. In all subjects a positive correlation was seen between Neuroticism and numbers of smoked cigarettes per day. Extraversion was negatively correlated with age in control and total group, but not in PD sample. There were significant correlations between Aggressiveness and age as well as onset of PD and number of cigarettes in PD group. Aggressiveness was negatively correlated with age in both control and total group as well as positively correlated with number of smoked cigarettes in total sample of subjects (Table 7).

Table 7. Correlation analyses of SSP factors in patient and control groups

	Neuroticism	Extraversion	Aggressiveness
PD group (n=193)			
Age (years)	r=–0.32; p=0.66	r=0.01; p=0.86	r=–0.16; p=0.03
Onset of PD (years)	r=–0.03; p=0.73	r=–0.04; p=0.60	r=–0.15; p=0.04
Education (years)	r=0.16; p=0.03	r=0.01; p=0.91	r=–0.03; p=0.72
Cigarettes (N)	r=0.09; p=0.24	r=0.02; p=0.81	r=0.18; p=0.01
Control group (n=314)			
Age (years)	r=0.05; p=0.43	r=–0.18; p=0.001	r=–0.23; p=0.000
Education (years)	r=0.10; p=0.08	r=0.02; p=0.79	r=–0.08; p=0.17
Cigarettes (N)	r=0.01; p=0.80	r=–0.01; p=0.86	r=0.11; p=0.06
All subjects (n=507)			
Age (years)	r=–0.03; p=0.46	r=–0.11; p=0.01	r=–0.21; p=0.000
Education (years)	r=–0.13; p=0.004	r=0.01; p=0.77	r=–0.07; p=0.11
Cigarettes (N)	r=0.10; p=0.02	r=0.00; p=0.97	r=0.17; p=0.000

6.2.6. Discussion

We presented the first study using SSP to show significant differences in the self-reported personality traits of patients with PD as compared to healthy subjects. Earlier, higher Neuroticism and probably lower Extraversion were found in patients with PD who were assessed with NEO or Maudsley Personality Inventory scales, whereas other personality traits were reported to be

similar to those in healthy subjects (Bienvenu et al., 2001a, Bienvenu et al., 2004, Carrera et al., 2006, Freire et al., 2007). As a personality pattern of PD patients has been characterised by higher rates of pathological personality traits compared to controls, our results showed a deviation of practically all SSP traits in patients with PD. We demonstrated that Neuroticism was the main personality characteristic of patients with PD, which was in a line with previous reports (Bienvenu et al., 2005, Freire et al., 2007, Zugliani et al., 2017). In particular, increased Somatic and Psychic Trait Anxiety and Stress Susceptibility were observed in all PD groups regardless of clinical status or phenotypes. By considering all personality traits simultaneously, Somatic Trait Anxiety stood out as the strongest predictor of the presence of PD. The SSP Somatic Trait Anxiety indicates a tendency to experience autonomic arousal; therefore, our findings are in line with the later developments of the tripartite model showing a specific link between heightened arousal and PD (Brown et al., 1998, Clark et al., 1994) as well as with the cognitive model of PD, which emphasises the role of increased interoceptive sensitivity and misinterpretation of somatic symptoms (Clark, 1986) along with the corresponding importance of anxiety sensitivity as a trait underlying the tendency for catastrophic misinterpretations of bodily changes (McNally, 2002).

Notably, the degree of Neuroticism correlated negatively with education level in both the PD group and the total sample of studied subjects, indicating that lower education may contribute to higher neurotic behaviour. One of the new findings was the significantly higher Aggressiveness among PD patients as compared to healthy subjects. Furthermore, the increased Aggressiveness was seen in both pure and comorbid PD groups, but it was more pronounced in the comorbid group, suggesting that aggression-related traits in PD may be associated with affective comorbidity. Another factor related to Aggressiveness in our sample was the presence of agoraphobia. Interestingly, PD patients with agoraphobia showed significantly higher Aggressiveness and particularly increased Trait Irritability than patients without agoraphobia. This finding suggests a link between the psychopathology of agoraphobia and trait Aggressiveness, which requires further research. In contrast to some of the previous studies, we found no difference in Extraversion between any of the studied PD groups and controls, suggesting that this personality aspect is probably less affected in PD.

Previous studies have proposed an accentuation of some personality traits, including Harm Avoidance, Neuroticism and Extraversion, in PD patients with affective comorbidity as compared with those experiencing pure PD (Ampollini et al., 1997, Bienvenu et al., 2001b, Freire et al., 2007). Similarly, Cuijpers et al. (2005) found Neuroticism to be the trait most strongly related to comorbidity. In our study, practically all SSP subscale scores were higher in patients with comorbid compared to pure PD. However, among SSP factors, only Neuroticism was higher among patients with comorbid panic phenotype. A number of clinical and demographic variables in our study were similar between PD only and comorbid groups, except the higher number of subjects with family psychiatric history among patients with affective comorbidity. Nevertheless,

none of the SSP traits or factors was significantly related to family psychiatric history. Thus, it is unlikely that increased Neuroticism in the comorbid PD group could be explained by these factors.

We also examined the relationships of personality traits to several demographic and clinical characteristics. The patients with current PD showed higher Neuroticism and related traits than PD patients in remission, but they did not differ in any other SSP trait or factor. Bienvenu et al. (2004) had also detected higher Neuroticism in patients with current PD compared to those in remission. Although high Neuroticism was proposed to predict the later onset of anxiety disorders (Bienvenu, 2007), none of the SSP personality traits significantly differed between patients with the earlier (<30 years) and late (>29 years) onset of PD in our sample. Previous studies have found that low Extraversion and low trust were associated with both agoraphobia and social phobia, but not with depression (Bienvenu et al., 2001a, Bienvenu et al., 2001b, Bienvenu et al., 2004). Furthermore, Carrera et al. (2006) have shown that PD patients were only more introverted than controls in the presence of agoraphobia. However, higher Neuroticism in patients with PD was prominent irrespective of agoraphobia. Furthermore, Openness, Agreeableness and Conscientiousness were unrelated to agoraphobia in their study. In our data set, neither Extraversion nor Neuroticism was related to agoraphobia. In respect to gender effects, Foot and Koszycki (2004), using NEO-PI-R, showed a lack of significant differences in anxiety sensitivity and Neuroticism scores between female and male PD patients with or without agoraphobia. However, women scored higher than men on Extraversion and men on angry hostility and depression facets of Neuroticism. In our study, none of the SSP traits was significantly affected by gender.

To the best of our knowledge, the sample of patients with PD in our study was to date the largest among the studies investigating personality traits in PD. However, certain limitations should be considered when interpreting our results. We were unable to account for the effects of treatment on personality traits in our sample. Notably, neither clinical severity nor short-term treatment response in PD was influenced by personality factors in an earlier study by Carrera et al. (2006). Both our findings and previous findings indicate that the expression of anxiety and stress-related traits may be state-dependent and intensified in the symptomatic stage of PD. We did not use specific clinical scales for the assessment of anxiety and panic severity. Although current PD would evidently be associated with more severe symptoms than PD in remission, the correlations between clinical and personality assessments should be addressed in more detail in the future. A possible confounder in our study was the small proportion of patients who met diagnostic criteria for bipolar disorder or (hypo)manic episode. Although this subgroup demonstrated personality traits consistent with non-bipolar groups (data not shown), the specific characteristics of PD with bipolar comorbidity need to be investigated in a larger sample.

6.3. Study III: Association between personality traits and escitalopram treatment efficacy in PD

6.3.1. Demographic and clinical characteristics

In present study, out of the 107 patients, who completed the study, 38 were diagnosed with PD (36%), 24 with PD and agoraphobia (22%), 14 with PD and co-morbid mild depression (13%) and 31 with PD, agoraphobia and mild depression (29%). The demographic characteristics of these groups did not differ significantly (Table 8). All 107 patients had a PDSS score higher than 7. At the beginning of the study, the mean score of PDSS was 16.07 and by the end of the study 5.16. By the end of study eighty-four (79%) patients met the criteria of remission.

Table 8. Demographic and clinical data

Variable	Mean or Frequency (n)	SD or %
Age (years; mean, sd)	34	11,73
Education (years; mean, sd)	13,7	2,5
Duration of PD (years; mean, sd)	7,7	9,5
Comorbid somatic diseases (n, %)	37	26
Gender (n, %)		
Male	36	34
Female	71	66
Occupation (n, %)		
Employed	70	67
Student	14	13
Retired	2	2
Unemployed	17	16
Disability	1	1
Smoking (n, %)		
Never	54	52
Formerly	22	21
Currently	28	27
Alcohol (n, %)		
Does not use	22	21
Once a month	39	38
2–4 times a month	35	34
2–3 times a week	8	8
Diagnoses (n, %)		
PD	38	36
PD and agoraphobia	24	22
PD and mild depression	14	13
PD, agoraphobia, and mild depression	31	29

6.3.2. Changes in SSP sub-scale scores following escitalopram treatment in PD

The means of all the T-scores of SSP sub-scales express tendency to decrease during the study. The largest changes were in Somatic Trait Anxiety (–6.59±9.98), Stress Susceptibility (–5.22±9.55), and Psychic Trait Anxiety (–5.13±8.18). The rest of the means of the scores of SSP sub-scales decreased less (Table 9).

Table 9. SSP sub-scale scores at visit 0 and visit 6, and the change of the scores

SSP sub-scale	Baseline; mean (sd) min…max	Study end; mean (sd) min…max	Difference; mean (sd) min…max1	*p*-value for difference
Somatic Trait Anxiety	65.91 (9.14) 45.02...89.41	59.32 (10.62) 34.06...86.8	–6.59 (9.98) –28.72...18.28	<0.0001*
Psychic Trait Anxiety	60.27 (9.67) 33.89...79.51	55.13 (9.55) 33.89...72.31	–5.13 (8.18) –31.21...24.01	<0.0001*
Stress Susceptibility	60.3 (10.59) 34.12...86.71	55.08 (11.06) 28.28...80.86	–5.22 (9.55) –26.29...37.98	<0.0001*
Lack of Assertiveness	52.43 (10.95) 23.43...77.58	49.52 (10.1) 26.4...80.57	–2.9 (8.48) –41.58...17.9	0.0009*
Impulsiveness	46.69 (11.51) 16.69...84.38	44.58 (11.38) 16.69...75.04	–2.11 (7.94) –26.83...18.67	0.0059*
Adventure Seeking	46.52 (10.13) 21.62...67.46	45.66 (10.18) 24.17...72.55	–0.86 (6.46) –20.81...13.01	0.3531
Detachment	50.16 (9.83) 24.05...73.69	49.45 (10.12) 23.68...70.57	–0.71 (6.88) –19.62...22.88	0.2695
Social Desirability	48.04 (10.35) 23.12...72.26	46.54 (10.51) 23.12...72.26	–1.51 (7.72) –28.08...14.04	0.0834
Embitterment	55.99 (10.48) 32.51...91.78	53.16 (11.12) 32.51...82.89	–2.82 (7.3) –23.72...11.86	0.0004*
Trait Irritability	57.17 (9.08) 32...77.35	53.91 (9.93) 26.78...75.08	–3.26 (7.08) –24.95...11.33	<0.0001*
Mistrust	53.62 (11.27) 28.14...89.21	51.68 (11.59) 25.22...83.44	–1.93 (9.22) –34.63...29.15	0.0240
Verbal Trait Aggression	52.52 (9.54) 28.55...75.99	51.09(9.7) 31.04...75.99	–1.42 (7.93) –44.88...14.96	0.1668
Physical Trait Aggression	52.37 (10.42) 33.11...84.02	51.77 (11.19) 30.72...86.54	–0.6 (6.85) –25.2...15.12	0.7796

* significant after Holm-Bonferroni correction for multiple comparisons

6.3.3. Correlation data

None of the baseline scores of SSP sub-scales was strongly associated with the treatment response. Only the Impulsiveness score was weakly correlated with the change of PDSS (r=0.22, p=0.033), and it helped to predict the odds for remission OR=0.90, p=0.005); however, these findings were statistically not significant after the adjustment for multiple comparisons (Table 10).

Table 10. Correlations between baseline scores of SSP sub-scales and change in PDSS and ratios of the odds of remission

SSP sub-scale	*r* (95% CI)	*P*	OR* (95% CI)	*p*
Somatic Trait Anxiety	0.05 (–0.16...0.24)	0.675	1.02 (0.93…1.03)	0.697
Psychic Trait Anxiety	–0.04 (–0.23...0.18)	0.818	1.00 (0.95…1.05)	0.928
Stress Susceptibility	0.04 (–0.16...0.24)	0.692	0.98 (0.96…1.05)	0.623
Lack of Assertiveness	0.01 (–0.18...0.23)	0.810	1.05 (0.95…1.04)	0.240
Impulsiveness	0.22 (0.03...0.41)	0.033	0.90 (0.88…0.97)	0.005
Adventure Seeking	–0.01 (–0.22...0.19)	0.895	1.02 (0.97…1.06)	0.590
Detachment	–0.03 (–0.24...0.16)	0.692	1.02 (0.97…1.06)	0.572
Social Desirability	–0.05 (–0.23...0.17)	0.766	1.04 (0.97…1.07)	0.254
Embitterment	0.00 (–0.18...0.23)	0.818	0.96 (0.91…1.00)	0.239
Trait Irritability	0.13 (–0.05...0.35)	0.142	0.94 (0.90…1.00)	0.152
Mistrust	0.09 (–0.11...0.29)	0.401	0.98 (0.91…0.99)	0.521
Verbal Trait Aggression	0.09 (–0.07...0.32)	0.222	1.00 (0.94…1.04)	0.898
Physical Trait Aggression	0.20 (–0.01...0.38)	0.064	1.00 (0.97…1.06)	0.999

* Adjusted for sex, age, years of education, level of drinking frequency, presence of somatic co-morbidities, and for the presence of mild depression and/or agoraphobia. The remission was defined if the score on the CGI improvement scale was 2 or less, the PDSS score 7 or less and no panic attacks had occurred for at least last two weeks.

Some weak correlations existed between the changes of the scores of SSP sub-scales and the changes in the clinical assessment scores. The change of SSP Stress Susceptibility was weakly correlated with the change of CGI-S (r=–0.27); the change of SSP Lack of Assertiveness was weakly correlated with the change of HAM-A (r=0.32) and EST-Q depression (r=0.21). However, none of the partial correlation coefficients was statistically significant after Holm-Bonferroni correction. (Table 11). The baseline scores of SSP sub-scales and the change in EST-Q depression score were not correlated. Similarly, neither changes in CGI-S scores nor changes in HAM-A scores were correlated with the baseline scores of SSP sub-scales. Partial correlations between Impulsiveness and change in CGI-S (r=0.29) and change in HAM-A (r=0.28) were statistically not significant after correcting for multiple testing (Table 12).

Table 11. Correlations between the changes of scores of SSP sub-scales and the changes of clinical assessment scores

	PDSS*	CGI-S*	HAM-A*	EST-Q depression*
Somatic Trait Anxiety	0.07 (–0.13...0.27)	–0.16 (–0.35...0.05)	0.24 (0.04...0.43)	0.03 (–0.18...0.23)
Psychic Trait Anxiety	0.11 (–0.09...0.31)	–0.09 (–0.29...0.12)	0.15 (–0.06...0.34)	0.10 (–0.10...0.30)
Stress Susceptibility	0.15 (–0.06...0.34)	–0.27 (–0.45...–0.07)	0.20 (0.00...0.39)	0.10 (–0.10...0.30)
Lack of Assertiveness	0.07 (–0.14...0.27)	–0.12 (–0.32...0.08)	0.32 (0.13...0.50)	0.21 (0.01...0.39)
Impulsiveness	–0.08 (–0.28...0.12)	0.07 (–0.14...0.27)	–0.07 (–0.27...0.14)	–0.02 (–0.22...0.18)
Adventure seeking	0.09 (–0.12...0.28)	–0.07 (–0.27...0.14)	0.09 (–0.12...0.29)	0.10 (–0.11...0.29)
Detachment	0.09 (–0.11...0.29)	0.02 (–0.18...0.23)	–0.01 (–0.22...0.19)	–0.09 (–0.28...0.12)
Social Desirability	–0.03 (–0.23...0.17)	0.09 (–0.12...0.29)	–0.02 (–0.22...0.19)	0.02 (–0.18...0.22)
Embitterment	0.16 (–0.04...0.35)	–0.17 (–0.36...0.04)	–0.01 (–0.21...0.19)	0.00 (–0.20...0.20)
Trait Irritability	–0.01 (–0.21...0.19)	0.06 (–0.15...0.26)	0.06 (–0.14...0.26)	0.04 (–0.17...0.23)
Mistrust	–0.05 (–0.25...0.16)	–0.02 (–0.22...0.19)	–0.07 (–0.27...0.14)	0.10 (–0.10...0.30)
Verbal Trait Aggression	–0.14 (–0.33...0.07)	0.07 (–0.13...0.27)	–0.06 (–0.26...0.15)	–0.15 (–0.34...0.05)
Physical Trait Aggression	–0.09 (–0.29...0.11)	0.03 (–0.17...0.24)	–0.13 (–0.32...0.08)	–0.10 (–0.29...0.11)

* *p*-values omitted; none of the *p*-values were statistically significant after Holm-Bonferroni correction for multiple comparisons. Adjusted for sex, age, years of education, level of drinking frequency, presence of somatic co-morbidities, and for the presence of mild depression and/or agoraphobia.

Table 12. Correlations between baseline scores of SSP sub-scales and changes in CGI-S, HAM-A, and EST-Q depression

	CGI-S		HAM-A		EST-Q depression	
	r (95% CI)	*p**	*r* (95%CI)	*p**	*r* (95% CI)	*p**
Somatic Trait Anxiety	–0.09 (–0.29...0.12)	0.407	–0.06 (–0.26...0.15)	0.608	0.03 (–0.18...0.22)	0.817
Psychic Trait Anxiety	–0.03 (–0.23...0.18)	0.806	0.04 (–0.17...0.24)	0.713	0.15 (–0.05...0.34)	0.152
Stress Susceptibility	–0.04 (–0.24...0.17)	0.740	0.11 (–0.10...0.30)	0.329	0.20 (–0.01...0.38)	0.063
Lack of Assertiveness	–0.08 (–0.28...0.13)	0.486	–0.08 (–0.28...0.13)	0.476	0.12 (–0.09...0.31)	0.278
Impulsiveness	0.30 (0.10...0.47)	0.005	0.29 (0.09...0.46)	0.007	0.06 (–0.15...0.26)	0.589
Adventure Seeking	0.04 (–0.17...0.24)	0.723	–0.04 (–0.24...0.17)	0.738	–0.13 (–0.33...0.07)	0.206
Detachment	–0.07 (–0.28...0.13)	0.493	0.03 (–0.17...0.24)	0.754	0.13 (–0.08...0.32)	0.234
Social Desirability	0.04 (–0.17...0.24)	0.744	–0.01 (–0.22...0.19)	0.915	–0.10 (–0.30...0.10)	0.326
Embitterment	–0.02 (–0.23...0.18)	0.838	0.09 (–0.11...0.29)	0.394	0.10 (–0.10...0.30)	0.342
Trait Irritability	0.18 (–0.03...0.37)	0.098	0.20 (0.00...0.39)	0.061	0.04 (–0.16...0.24)	0.712
Mistrust	–0.04 (–0.24...0.17)	0.727	0.23 (0.03...0.41)	0.032	0.09 (–0.11...0.28)	0.406
Verbal Trait Aggression	0.12 (–0.08...0.32)	0.256	0.14 (–0.07...0.33)	0.210	0.09 (–0.12...0.28)	0.408
Physical Trait Aggression	0.14 (–0.06...0.34)	0.186	0.28 (0.08...0.46)	0.008	0.03 (–0.17...0.23)	0.794

* uncorrected *p*-values; all were statistically not significant after Holm-Bonferroni correction for multiple comparisons; 95% confidence intervals and *p*-values, adjusted for sex, age, years of education, level of drinking frequency, presence of somatic co-morbidities, and for the presence of mild depression and/or agoraphobia.

6.3.4. Discussion

Several personality traits on the SSP measurement, including Embitterment, Impulsiveness, Lack of Assertiveness, Psychic and Somatic Trait Anxiety, and Stress Susceptibility, improved after 12 weeks of medication in comparison with the baseline scores. Although the changes in the SSP scores after the treatment period were generally more pronounced among remitters to escitalopram treatment compared to non-remitters, none of scores of the SSP significantly differed between these groups at the end of the treatment period. Moreover, no significant correlations were found between the changes of scores of SSP subscales and the changes of clinical assessment scores following 12 weeks of medication. These results look quite intriguing in the light of our previous study, which demonstrated the maladaptive personality disposition of practically all SSP traits in patients with PD (Võhma et al., 2010, Study II), confirming that maladaptive trait patterns may contribute to the development and expressions of PD. The current study suggests that antidepressant medication is accompanied by certain improvement in personality patterns in patients with PD, but changes in the traits do not seem to be clearly associated with treatment efficacy. Although our results may confirm the trait rather than state phenomena of personality deviations in PD, it is possible to speculate that personality characteristics are more flexible in terms of normalisation, at least among good responders to pharmacological intervention. The effect of antidepressant medication on personality traits in PD has not been univocally proven. None of the personality traits assessed by the Neuroticism-Extraversion-Openness Five-factor Personality Inventory was related to the short-term response to SSRI treatment in PD (Carrera et al., 2006). Still, a significant decrease was observed in all anxiety related traits after 6 months of treatment with SSRI citalopram in a smaller sample of PD patients, using the original scale for SSP measurement, the KSP (Neuger et al., 2002). Considering that a similar tendency to decrease SSP scores was found among our patients, we may suggest that a longer treatment period would probably reveal a statistically stronger effect of medication on personality traits. However, the more pragmatic explanation would be that the response to antidepressant medication and particularly the substantial decrease in clinical severity could also improve the self-rating of one's own personality characteristics.

The second main goal of our study was to detect the possible predictive effect of personality traits on treatment response to antidepressant medication. The only positive finding we detected, but which did not withstand Bonferroni correction for multiple comparisons, was the predictive effect of impulsivity. PD non-remitters to 12-week treatment with escitalopram showed a higher Impulsivity score at baseline SSP assessment compared with responders. SSP Impulsivity correlates with several constructs of the five-factor personality model. The strongest associations have been found with the Impulsiveness facet of Neuroticism and the Deliberation facet of Conscientiousness, thereby combining a low frustration tolerance with non-planning impulsivity (Aluoja et al., 2009).

Lower Neuroticism has predicted clinical improvement at three-month point in a Collaborative Care for Anxiety and Panic Study study (Chavira et al., 2009). The predictive effect of Impulsivity in our study was also confirmed by correlation analyses between SSP and the clinical scales scores. In particular, the higher score of Impulsivity at baseline was close-to-significantly associated with a lesser decrease in the CGI severity score during the treatment period. The same trends were also seen on the PDSS and HAM-A scales, but correlations did not reach statistically significant levels. Previously we reported that PD phenotype is characterised by a higher Impulsivity in comparison to normal presentation (Võhma et al., 2010, publication II). Nevertheless, the relationship between anxiety and impulsivity seems controversial (Barratt 1965; Askenazy et al., 2000). Our study accords with Marchesi et al. (2006) in finding that features of borderline personality disorder predicted a lower likelihood of remission with SSRIs in PD patients. Emotional instability and low impulse control are characteristic features of borderline personality, and they are also part of the Impulsivity construct measured by the SSP. Studies conducted with different methodologies have found no correlation between anxiety and impulsivity (Askenazy et al., 2000; Apter et al., 1993; Lecrubier et al., 1995; Caci et al., 1998). On the other hand, in several studies anxiety disorder patients have reported higher scores of impulsivity than healthy controls (Summerfeldt et al.,2004; Del Carlo et al., 2012). The possible involvement of impulsivity in treatment response appears to be less understood. Silva et al. (2010) demonstrated that borderline personality disorder carriers of long alleles of serotonin transporter promoter region related polymorphism (5-HTTLPR) had a better anti-impulsive response to SSRI fluoxetine treatment than in patients with short alleles. Walderhaug et al. (2010) also showed that reduced serotoninergic neurotransmission following acute tryptophan depletion increased impulsivity in healthy men, but decreased it in women. Considering that the relationship between reduced function of the central serotonin system and impulsivity is well recognised (Brown et al., 1979; Brown et al., 1982; Coccaro et al., 1989; O'Keane et al., 1992), we suggest that an increased impulsivity and worse anti-panic response to escitalopram treatment may indicate a more pronounced or persistent serotoninergic dysfunction, at least in the sub-group of patients with poor treatment outcome. Interestingly, significant and persistent changes in central serotonin functioning were observed by neuroimaging studies in male patients with PD (Maron et al., 2010b; Nash et al., 2008; Cannon et al., 2013). Nevertheless, none of these brain-imaging studies had measured the expression of the Impulsivity trait among their sample.

To the best of our knowledge, the sample of patients with PD in our study was to date the largest among the studies investigating the relationship between personality traits and treatment response in PD. However, certain limitations should be taken into account when interpreting our results. All patients were treated in a naturalistic way using an open-label drug, so placebo responses cannot be excluded; the control group is absent. However, to diminish possible sources of bias in variation in clinical assessments, the severity of PD symptoms

and treatment response were carefully rated by one experienced psychiatrist at each visit. Furthermore, all clinical assessments on the patients' self-reports on SSP measurements were made blindly. However, our sample size can still be considered not large enough to reveal statistically significant findings, especially keeping in mind several other factors, such as gender, age and co-morbidity.

7. GENERAL DISSCUSSION

According to our results, the Estonian version of the SSP has demonstrated high reliability and validity as evaluated in reference to both: the Swedish original data and the position of the SSP-measured traits within the basic personality dimensions of the five-factor model. Since the first introduction of SSP (Gustavsson et al., 2000), this scale has been applied in various mental health and somatic disorders, including depression, schizophrenia, bipolar disorder, cognitive disturbances, eating problems, psoriasis and others (Aluoa et al., 2018; Iliadis et al., 2015; Ausén et al., 2011, Elfhag 2005; Fagerberg et al., 2018; Rasul et al., 2016; Remröd et al., 2015; Sparding et al., 2017; Volgsten et al., 2010). The initial idea of developing KSP and its later modification with improved psychometric qualities, SSP, was to attain an instrument for evaluating personality traits in psychopathological groups. This was also the main reason for adaption of the Estonian version of SSP for several purposes, including the personality assessment in research and a clinical context. The SSP appears to be fairly stable in terms of repeated measures within the same individual groups (Hedman et al., 2014, Muller et al., 2015), and has shown similar factor loadings in different samples (Gustavsson et al., 2000, Fagerber et al., 2016, Volgsten H et al., 2010). The other advantage is its relatively short format, consisting of 91 items, as compared to 238–240 items for the full NEO and TCI questionnaires, which is an argument in favour of time effectiveness for SSP. Thus in line with earlier studies, the current work gives additional strong support for recommending the extensive use of SSP in further exploration of the role of personality factors in mental disorders.

It should be noted that the current work is the first implementation of SSP in investigation of personality traits in PD, which is very important in that the relationship between personality traits and PD is significantly less explored than the association of PD with personality disorders. We found that virtually all SSP traits show an abnormal range in patients with PD, while at least some personality aberrations seem to be more pronounced in PD with affective comorbidity compared to pure PD. Generally, the SSP factors of Neuroticism and Aggressiveness, but not Extraversion, were significantly higher in the PD group than in controls, and only a few demographic and clinical variables were associated with SSP scores in PD patients. These results add to the evidence of a maladaptive personality disposition in patients with PD, particularly high Neuroticism and manifest Somatic Trait Anxiety, which are probably not influenced by other clinically relevant factors. The associations between PD and both higher Neuroticism as well as lower Extraversion are in line with similar earlier observations (Bienvenu et al., 2001b, Bienvenu et al., 2004, Carrera et al., 2006, Freire et al., 2007). However, the finding of higher Aggressiveness and increased Trait irritability among PD patients, particularly with agoraphobia, as compared to healthy subjects seems very intriguing. In our previous study, we examined how personality disposition as assessed with SSP may affect the

response to the cholecystokinin tetrapeptide (CCK-4; 50 microg) challenge in healthy volunteers (n=105). Our results showed that the occurrence of CCK-4-induced panic attacks was best predicted by adhering to SSP-defined traits: Lack of Assertiveness, Detachment, Embitterment and Verbal Aggression. Moreover, for different subsets of CCK-4-induced symptoms, the traits of Physical Aggression, Irritability, Somatic Anxiety and Stress Susceptibility also appeared related to panic manifestations. In particular, higher Verbal trait Aggression predicted the occurrence of a panic attack, whereas increased Physical Trait Aggression predicted all aspects of panic symptoms (Toru et al., 2010). Previously, it has also been indicated that the tendency to be verbally aggressive was associated with a panic response to pentagastrin administration (Radu et al., 2003). The association between Aggressiveness and provoked panic response is further supported by George et al. (2000), who showed that persons exhibiting a high rate of physical aggression in domestic relationships react with more panic symptoms to sodium lactate provocation. The exact nature of these associations is unclear. A Radu et al. (2003) finding that personality emerges as a significant predictor of panic reaction only with a lower dose of pentagastrin suggests a rather non-specific stress reactivity. It is possible that certain personality traits heighten an individual's reactivity to different kinds of stressors, including panic-provoking agents. On the other hand, anxiety and aggression are known to share underlying neurobiology, including aspects of CCK neurotransmission and pharmacotherapy approaches (Siegel et al., 2007). Thus, our observation that Aggressiveness predisposes to a greater panic reaction in a laboratory challenge in healthy volunteers may indicate one relationship between traits of aggression and susceptibility to panic attacks. However, the relevance of these findings to clinical aspects of PD is not fully clear. Although an earlier study found that patients with PD reported significantly greater levels of anger aggression compared to controls (Moscovitch et al., 2008), this was not confirmed by other research showing a non-significant relationship between PD and aggression (Niazi et al., 2008). Interestingly, neither Physical nor Verbal traits of Aggression changed throughout the 12-week treatment with escitalopram in the current study, suggesting that aggressiveness is probably one of the endophenotypic features of PD.

Although several other personality traits, including Embitterment, Impulsiveness, Lack of Assertiveness, Psychic and Somatic Trait Anxiety and Stress Susceptibility, have improved on the SSP measurement after 12 weeks treatment with escitalopram, none of these positive changes significantly differed between remitters and non-remitters at the end of the treatment period. Furthermore, the lack of correlations between the changes in personality traits and the changes of clinical assessment scores following escitalopram treatment indicates that improvement in personality characteristics is probably contributed by the general effect of recovery resulting in better self-perception. Considering the earlier suggestion that the result of therapy can be attributed to the state level variance in personality trait measures (Du et al., 2002; Marchevsky, 1999), it would be tentative to speculate that SSP improvement following a treatment

period in PD can be temporally and may depend on the disease course. However, the recent meta-analysis conducted by Roberts et al. (2017) based on data from published studies in 1959–2013 and involving over 20,000 participants demonstrated that in comparison with other disorders such as depression, eating disorders, personality disorders and substance use, patients with anxiety disorders reported more pronounced and long-lasting changes in personality characteristics, especially in Neuroticism and Extraversion, just after a few weeks of therapy. In additional, a brief internet-based cognitive behaviour therapy (12 weeks) for severe health anxiety causes long-term changes in measures of SSP personality traits related to Neuroticism, whereas Extraversion and Aggression remained largely unchanged (Hedman et al., 2014). Interestingly, the stability of the SSP personality trait was also reasonably high among patients with psychotic disorders, although lower than among non-psychotic individuals in the study of Fagerberg (2018). On the other hand, Roberts et al. (2017) concluded by meta-analysis of earlier studies that psychopharmacological therapies actually exhibited a slightly smaller effect than the other treatment approaches, e.g. CBT, supportive therapy and psychodynamic methods, on changes of personality traits. This observation looks very intriguing in terms of further exploration of non-pharmacological therapy methods and their influence on SSP personality traits in PD patients.

The other dilemma raised from this study is the predictive effect of personality traits on treatment response to antidepressant medication in PD. The only personality trait that shows the possible predictive effect in current study was Impulsivity. In particular, a higher Impulsivity score at baseline SSP measurement in PD patients was associated with poor treatment outcome; however, no other SSP personality characteristics demonstrated a predictive effect. These results are in accordance with our recent study aiming to identify specific personality traits that could predict the treatment response and/or the dynamics of symptom change in 132 outpatients with major depressive disorders, who were also treated with escitalopram antidepressants for 12 weeks. We found that none of the studied SSP traits predicted the end result of the treatment. However, patients with higher Social Desirability, lower Stress Susceptibility and lower Irritability achieved a more rapid decrease in depression symptoms. Nevertheless, the latter associations did not survive the multiple testing corrections, probably due to the relatively small sample (Aluoja et al., 2018). Therefore, these findings suggest that specific personality traits may predict the trajectory of symptom change rather than the overall improvement rate, which is probably true for both highly co-existing mental disorders such as PD and depression. Notably, the lack of the major influence of SSP personality on the disease course was reported in patients with bipolar disorder, indicating that the personality profile does not seem to have prognostic value over a 2-year period in this type of mood disorder (Sparding et al., 2017).

Finally, it should be noted that genetic factors, not investigated in this study, should be considered when exploring the relationship between PD and personality traits. For example, there are recent findings showing that genetic poly-

morphisms, particularly within hydroxysteroid (11-beta) dehydrogenase 1 gene and the serotonin transporter gene-linked polymorphism 5-HTTPLPR, may modify manifestation of Neuroticism-related personality traits assessed by SSP (Iliadis et al. Gingnell et al., 2010). Although there is strong evidence that several genes may have a modulatory role on the onset, course and treatment outcome in PD, including among the Estonian population (Maron et al., 2010a), the genetic part was not included in this study due to the relatively small sample and risk of false findings; however, we recognise that the genetic impact on personality traits in PD requires further investigation.

8. CONCLUSIONS

1. We demonstrated that the SSP Estonian version has acceptable psychometric properties. The SSP measures traits that seem to be universal and are in line with the major theories of personality structure.
2. The use of SSP proved to add pertinent information on clinically relevant personality dimensions in patients with PD. We showed evidence of maladaptive trait patterns in patients with PD. In particular, these patients are characterised by high Neuroticism and higher manifestation of Somatic Trait Anxiety.
3. More pronounced personality trait deviations were observed in PD with affective comorbidity. Aggressiveness, in particular, was associated with agoraphobia and affective comorbidity.
4. Although maladaptive personality disposition in patients with PD shows a certain trend towards normalisation after a 12-week treatment with the antidepressant escitalopram, there was not a strong correlation with the clinical outcome. A better response to medication was accompanied by more pronounced improvement in personality characteristics, which is probably contributed by the general effect of recovery resulting in more positive self-perception.
5. The Impulsiveness shows a possible predictive effect on the antidepressant treatment response in PD, which seems intriguing and worthy of further investigation.

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SUMMARY IN ESTONIAN

Paanikahäirega patsientide isikuomaduste, kliiniliste näitajate seos farmakoloogilise ravivastusega

Sissejuhatus

Paanikahäire (PH) kui eraldiseisev häire lisati ametlikult psühhiaatriliste häirete nimistusse 1980. aastal DSM III publitseerimisel (APA, 1980). Paanikahäiret iseloomustavad korduvad paanikahood ning ootusärevus nende hoogude ees, sageli kujuneb sellest välja agorafoobia (DSM-IV, RHK-10).

Paanikahäire eluaegne esinemissagedus on 1.5–3.5%, kusjuures 12 kuu esinemissagedus on naistel kõrgem kui meestel (Klerman jt. 1991). PH algab tavaliselt kahekümnendate eluaastate keskel, naistel on leitud kõrgeim haaratus 25–34 eluaasta vahel, meestel 30–44 eluaasta vahel (Wittchen ja Essau, 1993).

PH kahjustab tõsiselt sotsiaalset toimimist, töö ja isikliku eluga toimetulekut, mõjutades seega oluliselt üldist elukvaliteeti (Candilis jt.1999). PH patsientidel on kalduvus tõlgendada kehalisi sümptomeid katastroofilisel moel, seetõttu on selle häirega isikute meditsiiniteenuste kasutamine ebaproportsionaalselt kõrge (Barsky jt. 1999), võrreldes kontrollvalimiga teevad nad oluliselt sagedamini visiite perearsti vastuvõtule (Simpson jt. 1994), kasutavad sagedamini vältimatut abi ja vaimse tervise abi võrreldes teiste üldmeditsiiniliste ambulatoorsete patsientidega (Barsky jt. 1999). PH loetakse üldiselt kroonilise kuluga häireks. Pikaaegses uuringus on kolme aasta järel leitud ainult 10% patsiente täielikult sümptomivabana (Noyes jt. 1990), täielik remissioon viie aasta pärast on leitud vaid 12% PH patsientidest (Faravelli jt. 1995).

Paanikahäire etiopatogenees on kompleksne, hõlmates sotsiodemograafilisi, geneetilisi, bioloogilisi ja psühholoogilisi faktoreid (Andrizano 2012, Wittchen ja Essau 1993, Scocco jt. 2007, Faravelli 1995, Tweed jt. 1989; Cougle jt. 2010, Goodwin jt. 2005b, Roy-Byrne jt. 1986; Assellmann jt. 2017, Hirshfeld-Becker jt. 2008). Paanikahäire ravis on kaksikpimedates uuringutes tõestanud efektiivsust viie ravimiklassi preparaadid: selektiivsed serotoniini tagasihaarde inhibiitorid (SSTI), serotoniini noradrenaliini tagasihaarde inhibiitorid, tritsüklilised antidepressandid, monoamiinioksüdaasi inhibiitorid ning bensodiasepiinid (Mitte, 2005; Bradwejn, 2005; Otto jt.2001; Gould jt. 1995; Susman &Klee 2005; Goddard jt.2001). Avaldatud uuringu kohaselt 20–40% paanikahäirega patsientidest ei anna ravivastust farmakoteraapiale ja 30–40% kognitiiv-käitumuslikule psühhoteraapiale (van Apeldoorn jt. 2008), seega mitte kõik patsiendid ei saavuta remissiooni.

SSTI-d leiti Otto (2001) ja kolleegide poolt läbi viidud 12 uuringut hõlmavas metaanalüüsis üldistunud ärevushäire ning paanikahoogude sageduse vähendamisel platseebost oluliselt efektiivsemad. Ka käesolevas uuringus on kasutatud paanikahäire raviks SSTI estsitalopraami 10–20 mg päevas.

Isiksust on kirjeldatud kui isiku unikaalset psühholoogiliste omaduse kogumit, mis väljendub läbi elu erinevates olukordades kindlates käitumismustrites (Gerrig

& Zimbardo, 2002). Isiksuse põhijooni on peetud elu jooksul stabiilseks, kuid viimastel aastatel on leitud, et need võivad läbi elu siiski muutuda seoses isiksuse küpsemisega või elusündmuste mõjul (Seviewright jt. 2002, Cohrs jt. 2008). Isiksuse omaduste, eriti neurootilisuse ja ekstravertsuse muutusi, on seostatud ka kliinilise sekkumisega (Roberts jt. 2017). On oletatud, et isiksus mängib otsustavat rolli paanikahäire alguse ning arengu juures (Clark, Watson, & Ineka, 1994). Paanikahäirega patsientidel on leitud kõrgenenud neurootilisust ja madalat positiivset emotsionaalsust (Bienvenu jt. 2001b; Bienvenu jt. 2004; Carrera jt. 2006; Zugliani jt. 2017). Madalat ekstravertsust on seostatud agorafoobiaga, mitte otseselt paanikahäirega (Bienvenu jt. 2004). Samas on leitud, et kõrgenenud neurootilisus ja madal ekstravertsus tulevad esile pigem komorbiidsuse korral (Cuijpers jt. 2005; Zugliani jt. 2013).

Paanikahäire ja isiksuse joonte seoste osas on mitu autorit avaldanud arvamust, et isiksuse jooni, eriti neurootilisust, võivad mõjutada nii häire ägedad sümptomid, farmakoteraapia kui ka kognitiiv-käitumuslik teraapia (Rocca jt. 2006, Corchs jt. 2008). Võrreldes depressiooniga on ärevushäirete, sealhulgas paanikahäire seost isiksuse omadustega vähem uuritud ja mõistetud (Bienvenu & Brandes, 2005). Neid seoseid on käsitletud kahepoolsetena, kus isiksus võib mõjutada ravitulemust ning ravi võib viia muutustele isiksuse mustris. On leitud, et isiksuse kõrvalekalded mõjutavad paanikahäire sümptomaatika intensiivust (Sokol jt. 1995, Ozkan jt. 2005) ja võivad negatiivselt mõjutada ravitulemust (Slaap&den Boer 2001; Marchesi jt. 2006). Samas on uuringuid, kus ükski NEO-PI-R-ga hinnatud isiksuse joon ei olnud seotud häire kliinilise raskuse ega lühiaegse ravitulemusega SSTI-ga (Carrera jt. 2006). Samuti ei leitud seost isiksuse joonte ja PH sümptomite remissiooni vahel (Marchesi jt.2006). Seega on uuringute tulemused isiksuse joonte mõjust paanikahäire ravitulemusele jäänud vastuoluliseks.

Hinnates PH farmakoloogilise ravi mõju isiksusele leiti, et sümptomite paranemisel vähenesid oluliselt ka neurootilisusega seotud isiksuse jooned (Reich jt. 1991; Noyes jt. 1986, Tang jt 2009, Barlow jt. 2013).

Kognitiiv-käitumisteraapia tulemusena leiti, et SSP-ga hinnatud neurootilised jooned vähenesid, samas ekstravertus ja agressiivsus jäid muutumatuks (Hedman jt. 2014). Märkimisväärne on, et kuigi on uuringuid, kus PH remissioon on seotud isiksuse joonte osalise "normaliseerumisega" (Brandes jt. 2006), on mitmeid uuringuid, kus isiksuse jooned jäävad stabiilseks kogu PH kulus (Morey jt. 2010, Santor jt.1997).

Uuringu põhjendus

Paanikahäire ja isiksuse seosed ei ole endiselt lõplikult selgitatud, see on jäänud teadusliku arutelu ja uurimise teemaks, sealjuures uuringute valimid on olnud suhteliselt väikesed ning tulemused vasturääkivad. Ärevushäirete, sealhulgas paanikahäire ravitulemust ennustavate tegurite parem tundmine aitab kaasa personaalmeditsiinile, patsiendile individuaalselt parima ravi valikuvõimalusele.

Isiksusel näib olevat ülioluline roll psüühikahäirete patogeneesis ja prognoosis. Oluline on ka see, et isiksuse omadused ravitulemuse ennustajana on kergesti hinnatavad. Käesolevas töös on kasutatud isiksuse hindamiseks Rootsi ülikoolide isiksuseskaalat (SSP), mille 13 alaskaalat on näidanud häid psühhomeetrilisi omadusi Rootsi normpopulatsioonis, kuid mis on eelkõige disainitud mõõtma isiksuse jooni psühhopatoloogia esinemisel (Schalling 1978; Gustavsson jt. 2000). SSP on tõestanud kasulikkust mitmetes psühhobioloogilistes uuringutes (Damberg jt. 2003, Jönsson jt. 2003). Faktoranalüüsi alusel mõõdab SSP kolme põhifaktorit: neurootilisus, ekstravertsus, agressiivsus (Gustavsson jt. 2000). Käesolevas uuringus kontrolliti SSP eestikeelse versiooni reliaablust ning valiidsust. See võimaldas hinnata SSP faktorite universaalsust originaalpopulatsioonist erinevas kultuuritaustas, samuti SSP suhet viiefaktorilise isiksusemudeliga.

Uurimistöö eesmärgid

Käesoleva töö üldine eesmärk oli kirjeldada paanikahäirega patsientide isiksuse omadusi ja uurida nende isiksuse joonte seoseid ravitulemusega, kasutades valideeritud SSP hindamisskaalat.

Kitsamad eesmärgid:

1. Kontrollida eestikeelse SSP reliaablust ja valiidsust (I)
2. Iseloomustada SSP-ga mõõdetud isiksuse joonte positsiooni viiefaktorilise isiksuse- mudeli suhtes (I)
3. Tuvastada paanikahäirega patsientide ja tervete isikute isiksuse joonte erinevused hinnatuna SSP-ga (II)
4. Uurida isiksuse omaduste erinevusi paanikahäirega patsientidel ilma ja koos afektiivse häirega ning jälgida paanikahäirel SSP domeenide (alaskaalad, üldfaktorid) ning erinevate demograafiliste ja kliiniliste muutujate vahelisi seoseid (II)
5. Uurida estsitalopraami ravi mõju paanikahäirega patsientide isiksuse joontele (III)
6. Leida, kas SSP-ga mõõdetud isiksuse omadused ennustavad paanikahäire farmakoloogilise ravi tulemust

Uuringutes osalejad ja meetodid

I uuringus osales 529 uuritavat. Esimeses grupis oli 331 tervet vabatahtlikku erinevatest uuringuprojektidest Tartu Ülikooli Psühhiaatriakliinikus ning teine grupp koosnes 198 erineva haridusliku ja sotsiaalse taustaga isikust. Mõlemas grupis osalejad täitsid Rootsi ülikoolide isiksuseskaala (SSP) (Gustavsson jt. 2000) ja 197 isikut teisest grupist täitsid NEO-PI-R (Costa &McRae, 1992b, Kallasmaa jt. 2000) eestikeelse variandi.

II uuringus olid kaasatud 193 paanikahäirega patsienti Tartu Ülikooli Psühhiaatriakliinikust ning 314 ajalehekuulutuse kaudu leitud tervet vabatahtlikku.

Paanikahäirega patsientidest 71 olid ainult paanikahäirega, 122 komorbiidse paanikahäirega, kusjuures 93-l esines kaasuvana depressioon, 29-l bipolaarne häire, 46-l teised ärevushäired, sealhulgas obsessiivne-kompulsiivne häire ja sotsiaalfoobia. Agorafoobia esines kaasuvalt 115-l, sealhulgas ainult paanikahäirega grupis 46-l ja komorbiidse häirega grupis 69-l. Kõik patsiendid ning tervete kontrollgrupp täitis SSP eestikeelse variandi.

III uuringus osales lõplikus valimis 107 paanikahäirega patsienti, kes täitsid SSP algvisiidil ning 12-nädalase ravi järel 10–20 mg estsitalopraamiga. Kaasuvalt täitsid uuritavad algvisiidil ning iga järgneva kahe nädala järel lisaskaalad PDSS (Shear jt. 1997), CGI (Guy 1976), HAM-A (Hamilton 1959), emotsionaalse enesetunde küsimustiku (EEK-2) (Aluoja jt. 1999), TSES (Vanderkooy jt. 2002).

Kõikides uuringutes tõendati paanikahäire ja teiste häirete olemasolu või puudumist kliinilise intervjuu ning rahvusvahelise neuropsühhiaatrilise intervjuu MINI (M.I.N.I. 5.0.0; Sheehan jt. 1998) läbiviimisega.

Peamised tulemused

Esimeses uuringus olid SSP alaskaaladest naistel oluliselt kõrgemad väärtused psüühilisel ärevusel, vastuvõtlikkusel stressile, kehtestavuse puudumisel ja sotsiaalsel soovitavusel. Meestel olid kõrgemad näitajad verbaalsel ja füüsilisel agressioonil, umbusklikkusel ja seikluste otsimisel. Suurimad soolised erinevused ilmnesid agressiooni ja ärevuse alaskaaladel.

Rootsi ülikoolide isiksuseskaalal (SSP) leiti kolmefaktoriline struktuur.

Esimene faktor hõlmas skaalasid, mis iseloomustavad neurootilisust, kirjeldades ära 27,8% andmete koguhajuvusest. Kõige suurema faktorlaadungiga selles faktoris olid somaatiline ja füüsiline ärevus, vastuvõtlikkus stressile, kehtestavuse puudumine.

Teine faktor kirjeldas 20,2% andmete koguhajuvusest. Faktori moodustasid alaskaalad verbaalne ja füüsiline agressiivsus, ärrituvus, isoleerumine ja madal sotsiaalne soovitavus, osutades agressioonile ja mittekonformsusele. Kusjuures isoleeritus ja ärritatavus haakusid ka esimese ja kolmanda faktoriga.

Kolmas faktor kirjeldas ära 14,8% andmete koguhajuvusest. Kolmandasse faktorisse kuulusid impulsiivsus ja seikluste otsimine.

Umbusklikkus haakus lähedaselt kahe faktoriga, mis mõõtsid neurootilisust ning agressiooni.

Seega faktoranalüüs kinnitas eestikeelse skaala kolmefaktorilist struktuuri sarnaselt esialgsele Rootsi normatiivile: neurootilisus, agressiivsus ja ekstravertsus.

Eestikeelse NEO-PI-R neurootilisuse dimensioon korreleerus kõige tugevamalt SSP neurootilisuse faktoriga. NEO-PI-R ekstravertsus korreleerus positiivselt SSP alaskaalade seikluste otsimise ja impulsiivsusega ning negatiivselt isoleerumise, psüühilise ärevuse, kehtestavuse puudumise, vastuvõtlikkusega stressile ning umbusklikkusega. NEO-PI-R faktor sotsiaalsus korreleerus positiivselt SSP alaskaala sotsiaalse soovitavusega, negatiivselt agressiivsuse-

ärrituvuse, umbusklikkuse ja kibestumisega. NEO-PI-R faktorid meelekindlus ja avatus olid nõrgemalt seotud SSP-ga. NEO-PI-R meelekindlus korreleerus kõige enam SSP sotsiaalse soovitavuse ja avatuse faktor seikluste otsimisega. Kokkuvõtvalt, NEO-PI-R ja SSP uurimine kinnitas viimase skaala valiidsust. Erinevused kahe skaala vahel võivad olla tingitud sellest, et SSP on võrreldes NEO-PI-R-ga spetsiifilisema suunaga, püüdes kirjeldada isiksuse patoloogilisi nüansse.

Kokkuvõtvalt näitas SSP eestikeelne versioon kõrget reliaablust ja valiidsust kõrvutatuna Rootsi originaalvalimiga ning ka viiefaktorilise isiksusemudeliga.

Teises uuringus ei olnud olulisi erinevusi patsientide ja kontrollgrupi demograafilistes näitajates. Komorbiidse PH patsientidel oli enam psüühilisi häireid perekonna anamneesis võrrelduna ainult PH patsientidega, samuti oli komorbiidses PH grupis rohkem suitsetajaid. SSP alaskaalade analüüsis leiti PH patsientide ja tervete kontrollgrupi isiksuse omaduste vahel erinevused. Kõik SSP alaskaalad, välja arvatud isoleerumine ja füüsiline agressioon, olid PH patsientidel oluliselt nihkes võrreldes kontrollgrupiga, sealhulgas seikluste otsimine ja sotsiaalne soovitavus madalamad, kõik teised alaskaalad kõrgemad. SSP faktorid neurootilisus ja agressiivsus, kuid mitte ekstravertsus, olid oluliselt kõrgemad PH grupis võrreldes kontrollgrupiga.

Komorbiidse paanikahäire ning kontrollgrupi võrdluses leiti oluline erinevus kõigis SSP alaskaalades, välja arvatud seikluste otsimine. Kõik alaskaalad olid komorbiidse PH grupis kõrgemate väärtustega, välja arvatud sotsiaalne soovitavus, mis oli madalam. Ainult PH patsiendid demonstreerisid kõrgemat neurootilisust ja agressiivsust, kuid ekstravertsus oli sarnane kontrollgrupiga.

Kahe paanikahäirega patsientide grupi võrdluses olid nihked rohkem väljendunud komorbiidse PH grupis, erinevus leiti ärevuse alaskaalade, stressile vastuvõtlikkuse, kibestumise ja ärritatavuse skaaladel. Kolmest faktorist erines kahe PH grupi vahel ainult neurootilisus.

Käesoleva paanikahäirega grupis võrreldes remissioonis patsientidega olid oluliselt kõrgemad väärtused ärevuse alaskaaladel ja stressile vastuvõtlikkusel, kuid mitte teistel skaaladel. SSP faktoritest oli ainult neurootilisus oluliselt kõrgem käesoleva PH patsientidel.

Käesoleva PH-ga patsiendid näitasid võrreldes kontrollgrupiga olulist erinevust mitmel SSP alaskaal, välja arvatud impulsiivsus, isoleeritus ja füüsiline agressioon.

Seega võib uuringu tulemusel väita, et paanikahäirega patsiente iseloomustavad väheadaptiivsed isiksusejooned, eriti kõrge neurootilisus ning tugev kalduvus somaatilisele ärevusele.

Kolmandas uuringus leiti kõigi SSP alaskaalade T-skooride langemine 12 nädalase farmakoloogilise ravi järel võrreldes algväärtusega, kuid ükski muutus ei olnud statistiliselt olulisel tasemel. Kõige rohkem vähenesid somaatiline ärevus, vastuvõtlikkus stressile ja psüühiline ärevus.

Leiti mõned nõrgad, statistiliselt mitteolulised seosed SSP alaskaalade ja kliinilise seisundi hinnangu skaalade vahel.

Ükski SSP alaskaalade algväärtusest ei olnud oluliselt seotud ravivastusega. Ainult kõrgem SSP impulsiivsuse tase uuringu alguses oli lähedal statistiliselt olulisele ennustamaks remissiooni mittesaavutamist peale 12 nädalast ravi estsitalopraamiga. Algse impulsiivsuse tase oli statistilisele olulisele lähedaselt seotud ka CGI, HAM-A ja PDSS väiksema langusega raviperioodil.

Järeldused

1. Demonstreerisime, et SSP eestikeelne versioon näitas aktsepteeritavaid psühhomeetrilisi omadusi. SSP mõõdab isiksuse jooni, mis on universaalsed ja haakuvad ühe varasema juhtiva isiksuseteooriaga.
2. SSP suutis lisada asjakohast informatsiooni kliiniliselt olulistele isiksuse dimensioonidele paanikahäirega patsientidel. Me näitasime, et PH patsientide isiksuse struktuur on madala adaptiivsusega. Neid patsiente iseloomustab eelkõige kõrge neurootilisus ja somaatilise ärevuse väljendumine.
3. Enam väljendub isiksusejoonte kõrvalekalle afektiivse komorbiidsusega paanikahäirega patsientidel. Agressiivsus oli seotud agorafoobia ja afektiivse komorbiidusega.
4. Kuigi PH patsientide madala adaptiivsusega isiksus näitas kindlat suunda normaliseerumisele 12-nädalase antidepresssandi estsitalopraami raviga, ei leidnud me isiksusejoonte olulist seost kliinilise ravitulemusega. Parema farmakoloogilise ravivastusega kaasnes enam väljendunud paranemine isiksuse joontes, mida võib omistada üldiselt paremale enesetunnetusele paranemisel.
5. Võimalikku ennustavat efekti PH ravis antidepressandiga näitas impulsiivus, mis näib huvipakkuv ning vajab edasist uurimist.

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PUBLICATIONS

CURRICULUM VITAE

Full name	Ülle Võhma
Date of birth	February 23, 1963
Citizenship	Estonian
Employment	North Estonia Medical Centre Foundation Psychiatric Clinic
Address	52 Paldiski Rd, Tallinn 10614, Estonia
Phone	+ 372 617 25 00
E-mail	ylle.vohma@regionaalhaigla.ee

Education:

1999–2017	University of Tartu, Department of Psychiatry, doctoral student
1996–1999	University of Tartu, Faculty of Medicine, residency in psychiatry
1991–1995	University of Tartu, Faculty of Philosophy, Speciality: Psychology Baccalaureus Scientiarum
1981–1987	Universtity of Tartu, Faculty of Medicine, Department of Paediatry

Scientific work:

My research interest has been focused on panic disorder and on the association of the disorder with personality traits

Working Experience:

2002–	North Estonia Medical Centre Foundation Psychiatric Clinic, Psychiatrist, Senior Doctor, The Head of Department
1999–2002	Tallinn Psychiatric Hospital, Psychiatrist
1988–1996	Tallinn Pelgulinna Hospital Children Outpatient Deprartment, Paediatrician

Publications:

Võhma, Ü.; Raag, M.; Tõru, I.; Aluoja, A.; Maron, E. (2017). Association between personality traits and Escitalopram treatment efficacy in panic disorder. *Nordic Journal of Psychiatry*, 71 (6), 433–440.

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Membership in professional organizations:

Estonian Association of Psychiatrists

ELULOOKIRJELDUS

Nimi:	Ülle Võhma
Sünniaeg:	23.02.1963
Kodakondsus:	Eesti
Praegune töökoht:	SA PER Psühhiaatriakliinik
Aadress:	Paldiski maantee 52/6, 10617 Tallinn
Telefon:	+ 372 617 25 00
E-post:	ylle.vohma@regionaalhaigla.ee

Haridus:

2009–2017	Tartu Ülikool, arstiteaduskond, psühhiaatriakliinik, doktoriõpe
1996–1999	Tartu Ülikool, psühhiaatria residentuur
1991–1995	Tartu Ülikool filosoofiateaduskond: psühholoogia eriala *baccalaureus scientiarum*
1981–1987	Tartu Riiklik Ülikool, pediaatria eriala

Teadustöö:
uurimistöö on põhiliselt keskendunud paanikahäirele ja selle seostele isiksusejoontega

Töökogemus:

2002–	SA Põhja Eesti Regionaalhaigla Psühhiaatriakliinik psühhiaater, vanemarst, osakonna juhataja
1999–2002	Tallinna Psühhiaatriahaigla, psühhiaater
1988–1996	Tallinn Pelgulinna Haigla Kalamaja Lastepolikliinik, pediaater

Publikatsioonid:

Võhma, Ü.; Raag, M.; Tõru, I.; Aluoja, A.; Maron, E. (2017). Paanikahäirega patsientide isikuomaduste seos estsitalopraami ravi efektiivsusega. *Nordic Journal of Psychiatry*. 71 (6): 433–440.

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